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SURGERY

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SURGERY

VOL. 26 NOVEMBER, 1949 No. 5

Original Communications

THE HUMAN HEART RATE

SOME OBSERVATIONS AND DEDUCTIONS BASED UPON THE EFFECT OF REMOVING PORTIONS OF THE SYMPATHETIC NERVOUS SYSTEM IN MAN

R. H. SMITHWICK, M.D., E. M. CHAPMAN, M.D., D. KINSEY, M.D., AND G. P. WHITELAW, M.D., BOSTON, MASS.

CHAPMAN, Kinsey, Chapman, and Smithwick,[1] in 1948, presented their preliminary observations on the effect of removing the motor pathways through which the cardioaccelerator fibers are transmitted to the human heart. They concluded that removal of the right and left second, third, fourth, and fifth thoracic sympathetic ganglia produced a marked reduction in basal pulse rate as well as a diminished acceleration following exercise, and hence motor pathways (cardioaccelerator fibers) to the human heart appeared to be derived from both the right and left second, third, fourth, and fifth thoracic sympathetic ganglia. It was suggested that this procedure might be of therapeutic value in the control of tachycardia and possibly other disturbances of cardiac rhythm in selected patients. The data to be presented in this paper more thoroughly substantiate these original conclusions.

Von Bezold[2] in 1863, Hunt[3] in 1899, and Krogh and Lindhard[4] in 1913 made major contributions to our knowledge of the vagus effect on the heart rate as well as the manner in which this effect occurs. In addition, Hunt[3] studied extensively the action of cardioaccelerator nerves to the heart, in animal experimentation, and demonstrated tonic activity of the accelerators. However, it must be remembered that work done on the cardiac accelerator mechanism prior to the paper of Cannon and associates in 1926 did not take into consideration the existence of cardio-accelerator fibers below the first dorsal ganglion.

Langley[5] in 1892 demonstrated that accelerator impulses to the heart leave the cord by the upper five pairs of anterior roots and their white rami. He was in error, however, regarding the transmission of these impulses through the cervical cardiac nerves. Cannon and associates[6] in 1926 demonstrated in animals that accessory cardiac accelerator fibers are carried to the heart in branches of the thoracic sympathetic nerves that lie below the

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stellate ganglion. This important observation was soon verified by Braeucker[7] and Ionescu, Enachescu and Teitel.[8] Kuntz and Morehouse[9] demonstrated by anatomic dissections on post-mortem human hearts that cardioaccelerator nerves direct to the human heart come from the second, third, fourth, and fifth thoracic ganglia of the sympathetic nervous system. Saccomanno, Utterback, and Klemme[10] confirmed these findings in dogs by using a special preparation and recording the effect of stimulating various upper thoracic nerves.

White and Bland, 1948,[11] stated, "Concerning the interruption of motor impulses which drive the heart to exceed its limited capacity for work, the experiments of White, Garrey and Atkins showed that to accomplish this it is necessary to perform extensive upper thoracic ganglionectomy on both sides. It is also necessary to eliminate the secretion of the adrenal medullas, because Cannon, Lewis and Britton have found that the denervated heart is accelerated by minute quantities of adrenine. If it were practical to do this, the heart would be seriously crippled thereby. Our clinical observations have shown that all the sympathetic cardiac nerves can be interrupted and still permit the heart an adequate accelerator response through reduction in vagal tone and the chemical mediation of adrenine and sympathin."

There is apparently some confusion in the literature regarding the terms "sympathectomized" and "denervated" as applied to the heart. Indeed, the denervated heart may be accelerated by minute quantities of adrenine, but in any case there is no confirmation of this in the paper of Cannon and coworkers, 1926. Even though the denervated heart were accelerated by minute amounts of circulating adrenine and sympathin, it would not necessarily follow that the sympathectomized heart would be accelerated likewise by minute amounts of adrenine and sympathin, as the vagal tone might well counterbalance any effect of the chemical mediators.

Chapman, Kinsey, Chapman, and Smithwick[1] inferred that White and Smithwick,[12] on page 281 of their book, said "that by total sympathectomy 'the heart would be undoubtedly greatly crippled.'" What White and Smithwick[12] actually meant was that by total cardiac denervation plus adrenalectomy, or adrenal denervation, "the heart would undoubtedly be greatly crippled." There is no doubt that this would be the case. Such a procedure, of course, would be out of the question to consider in man.

Chapman, Kinsey, Chapman, and Smithwick[1] stated that, "The effect of sympathectomy on heart rate was no greater in those patients who had splanchnic denervation supposedly including the adrenals than those who had cardiac (2nd to 5th dorsal ganglion) denervation only." This matter will be more fully discussed in a separate communication in the near future and the summary of our clinical observations given at that time.

In 1936, Brouha, Cannon, and Dill[13] showed that totally sympathectomized dogs run, jump, play, and look like normal dogs, and yet after exercise their pulse rates were 30 to 40 per cent below those of normal dogs. In 1938, Smithwick had done a total sympathectomy on a hypertensive man

without ill effects and noted that bradycardia was present. Adson and Brown[14] reported that they had not observed any diminution of pulse acceleration after effort when the first two thoracic ganglia bilaterally had been severed in one case.

An objection to cardiac sympathectic denervation might be raised in reference to possible adverse effects on coronary circulation, particularly in cases of angina pectoris. The controversial question of the innervation of the coronary vessels has not as yet been answered. Anrep and Segall,[15] by use of a complicated preparation in a dog, reached the conclusion that the sympathetic nerves caused coronary vasodilatation whereas stimulation of the vagus nerves caused coronary vasoconstriction. Kountz, Pearson, and Koenig[16] in working with revived human hearts were not able to support the conclusions of Anrep and Segall. Katz and Jochim[17] in studying the innervation of the coronary vessels of the dog found that stimulation of the sympathetic nerves to the coronary vessels predominantly produced vasoconstriction. It will be seen, therefore, that different workers in this field have reached diametrically opposed conclusions. From a practical standpoint, patients who have had sympathetic cardiac denervation have not had any adverse effect on the coronary circulation in so far as has been determined from a clinical evaluation of our cases.

The idea leading to the observations of Chapman, Kinsey, Chapman, and Smithwick[1] came from patients who had thoracic sympathetic nerves severed for other indications and later noted that their pulse rate was slower and that exercise did not cause as marked an increase in heart rate as before sympathectomy. Attention was thereby directed to the possible control by surgical methods of disabling exertional or emotional tachycardia and other disturbances of cardiac rhythm. Nineteen patients who had thoracic sympathetic ganglia removed from one or both sides were discussed in their paper.

Clinical Material.—This present report deals with the effect on the pulse rate of thirty-seven patients who have had different portions of the thoracic sympathetic chain removed from one or both sides for various purposes, such as disabling emotional or exertional tachycardia, angina pectoris, coronary artery heart disease, with or without associated hypertension, vasomotor disorders of the upper extremities, and hyperhidrosis with or without vasomotor involvement. These studies were done on the pulse rate response to exercise of patients before and then at intervals after removal of the thoracic sympathetic ganglia, first on one side and later after the second stage on the opposite side. The pulse rate recordings were obtained from a slight modification of the "two-step" exercise test as described by Master, Nuzie, Brown, and Parker.[18] This is described later in more detail. The levels of resection were later verified by x-ray identification of clips left at the operative site, by the presence or absence of Horner's sign, by skin resistance studies, and by surface temperature determinations.

From March, 1946, until March, 1948, 117 patients had thoracic sympathectomy performed by us for one of the aforementioned reasons. Most of the procedures have been bilateral at separate stages, making a total of 199 opera-

tions in all. The operative mortality was .85 per cent per patient and .5 per cent per operation. Of the 199 operations, 67 were extrapleural. There were no operative deaths in this group. The operative risk for these procedures will be discussed in more detail in a later paper. All of the patients operated upon are not included in this present study owing to incomplete data as to the effect on the heart rate on those patients operated upon for other indications.

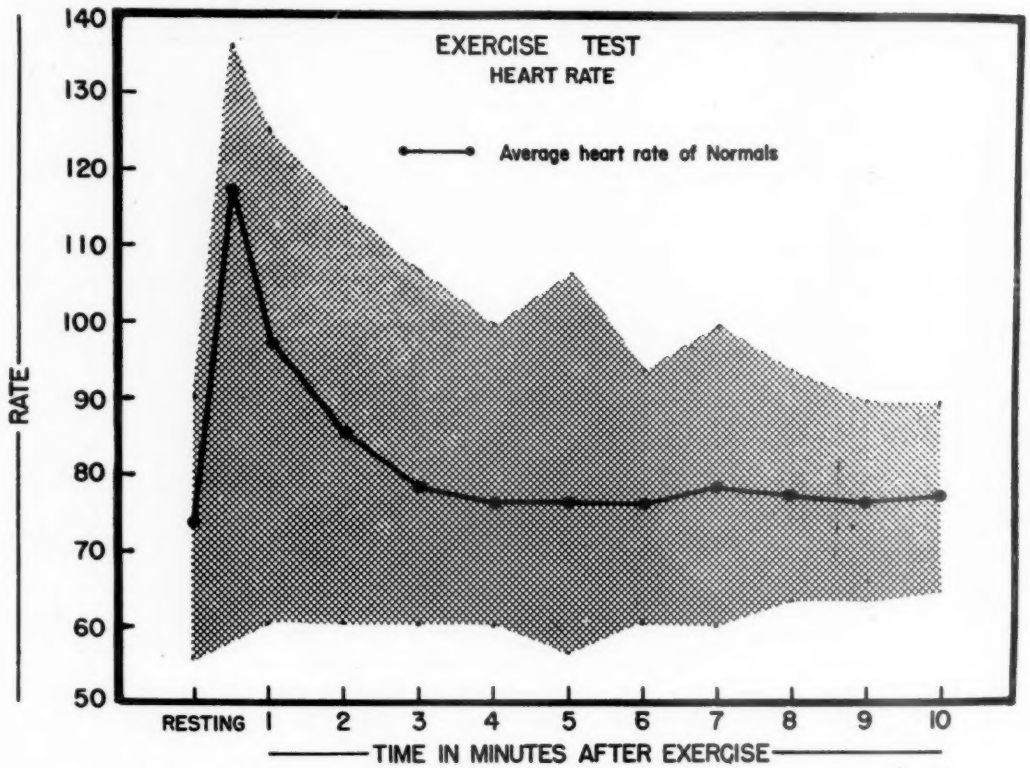

Fig. 1.—Normal response of a series of thirty-five young, healthy, supposedly normal individuals to the modified "two-step" Master exercise test.

Observations.—Observations of heart rate were made in forty-six patients undergoing various operative procedures. Two varieties of exercise tests were employed. In the majority of cases a slight modification of the technique described by Master and co-workers[18] was utilized. In brief, this test is performed as follows: After a period of reclining in a recumbent position, until the heart rate is essentially constant, the patient walks up and down two steps, each 9 inches high, a certain number of times in one and one-half minutes. The number of times is determined by a chart compiled by Master and associates on the basis of the age, sex, and weight of the patient. The pulse rate was recorded before and immediately after the test and then at one-minute intervals, for ten minutes. The rate recorded before the test is listed as the "resting rate" and the rate recorded immediately after the test is listed as the "maximal rate" in the tables. This test was found to furnish an ade-

quate stimulus for cardiac acceleration, and did not exceed the exertional capacity of patients who had coronary heart disease with angina pectoris or hypertension or both. In a few patients, a more strenuous test devised by one of us (E. M. C.) was used. In this, after a preliminary rest period, the patient steps up and down one 16-inch step thirty times in one minute. Control observations for each test were made in two series of young, healthy, supposedly normal individuals. These are illustrated by Figs. 1 and 2. The top of the crosshatched area indicates the highest rates of the various individuals of the series and the bottom of the crosshatched area indicates the lowest rate of the individuals used in this series. The heavy solid line is the

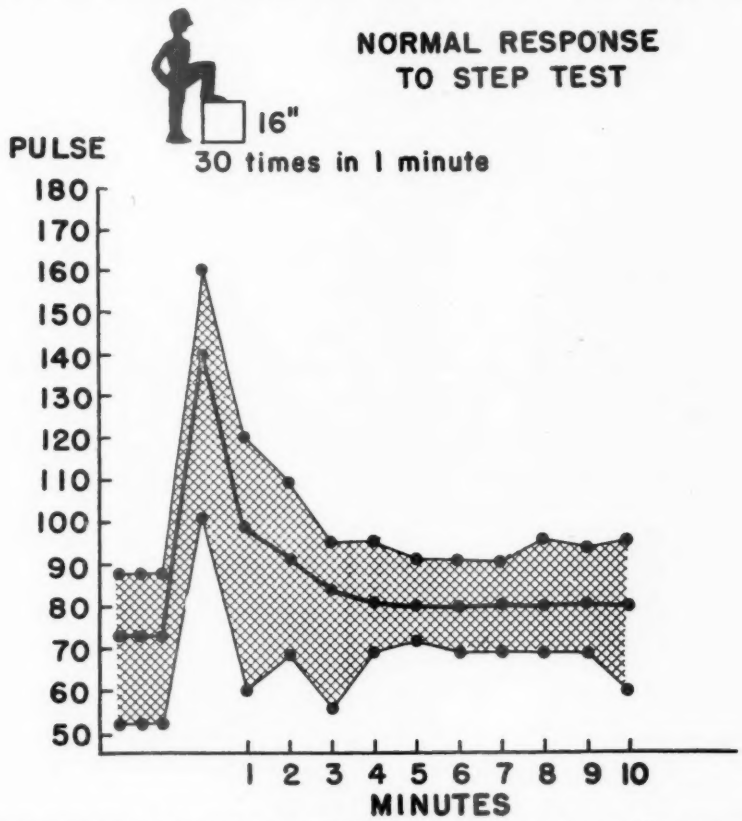

Fig. 2.—Normal response of a series of fifteen young, healthy, supposedly normal individuals to the modified "one-step" exercise test.

average of all those tested. These tests were performed before, after unilateral and after bilateral procedures in the great majority of patients, and before and after both operations in a few. The data furnish information concerning the neurogenic control of the human heart rate and are of a variety previously unavailable except for a preliminary report by several of us[1] concerning this matter. We were particularly interested in obtaining further information bearing upon the origin of the cardioaccelerator fibers from the cord, the relative effect of unilateral and bilateral cardiac denervation, the role of the parasympathetic and the sympathetic divisions of the autonomic nervous system in the control of the resting heart rate and of the accelerator

response to exercise, and possible clinical application for cardiac denervation (sympathetic motor).

Information bearing upon these matters was obtained by grouping patients according to the operative procedure performed and studying the re-

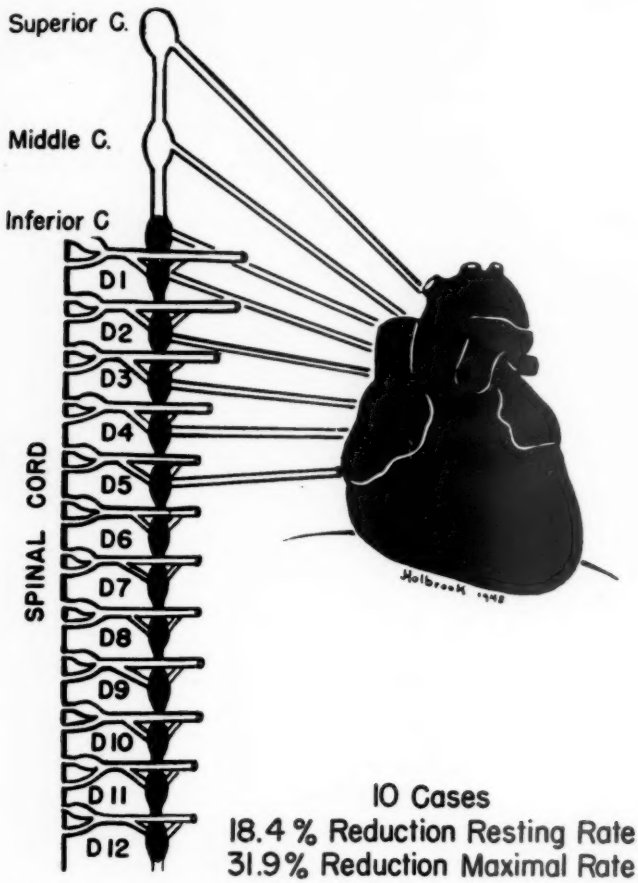

Diagram 1.—Effect of removing inferior cervical or D_1 through D_{11} or D_{12} inclusive in ten cases.

sults of the step test before and after each operation. Data having to do with the upper limit of the sympathetic outflow from the cord are summarized in Table I. The effect of bilateral operations in twenty-one cases upon the control heart rate and the maximal, the two-minute, five-minute, and ten-minute

TABLE I

GROUP	NO. CASES	OPERATION	EFFECT	RESTING	MAXIMAL	2 MIN.	5 MIN.	10 MIN.
1	10	Inf. C or T_1 to T_{11} or T_{12} inclusive	% Reduction	18.4	31.9	16.3	22.8	21.5
2	10	T_2 to T_{11} or T_{12} inclusive	% Reduction	21.3	31.7	27.7	26.5	24.6
3	1	T_3 to T_{11} or T_{12} inclusive	% Change	+2.3	+12.0	+3.4	−2.4	0.0

The data in this table have to do with the upper level of outflow of the cardioaccelerator fibers from the thoracic cord. They indicate that the outflow from the first thoracic segment in man is not important but that the outflow from the second segment is important and probably is the upper level. All operations were performed bilaterally.

rates after exercise, is expressed in terms of percentage reduction in rate after the different procedures. The first group consists of ten cases in which all possible connections between the cord and the heart were removed. This is shown schematically in Diagram 1. In this and subsequent diagrams, the blacked-out ganglia represent those removed. In these cases, the upper limit of the resection included the inferior cervical or the first thoracic ganglion or both, and the lower limit extended as low as the eleventh or twelfth thoracic ganglion, inclusive (see Fig. 3). The second group consists of ten

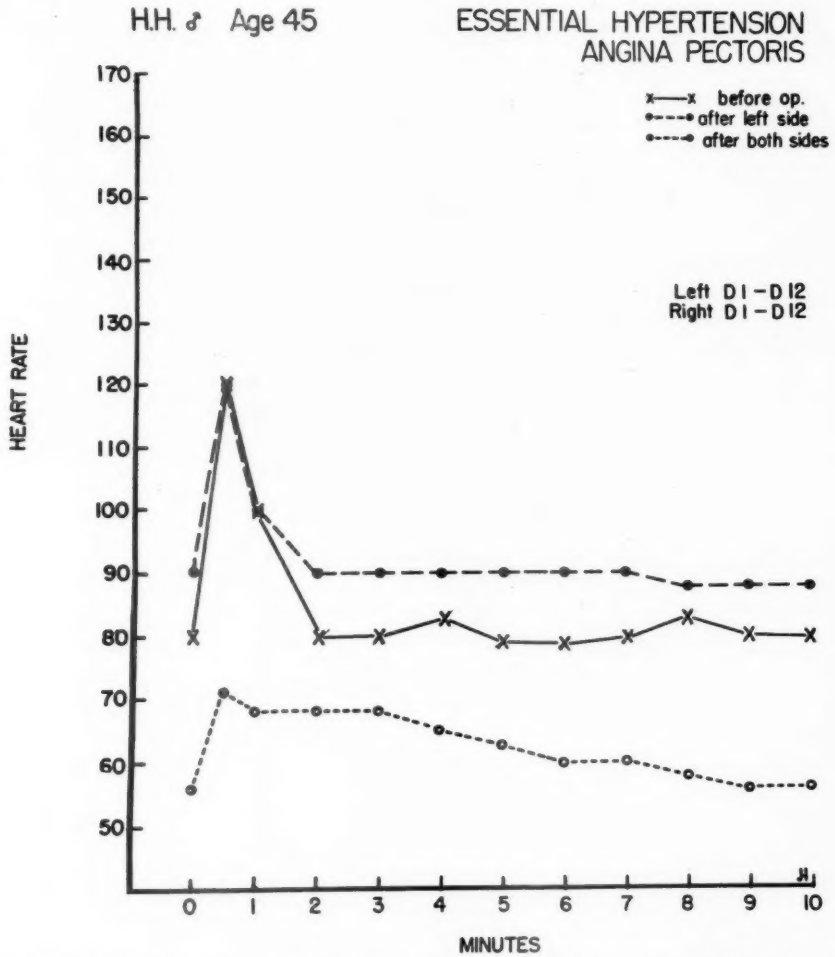

Fig. 3.—The exercise test in a case of hypertension combined with angina pectoris.

cases in which the upper limit included the second thoracic ganglion and the lower limit was the same as in the first group. (See Diagram 2, Fig. 4, and Table I, Group 2.) The only difference between the operations in the two groups was that any cardioaccelerator fibers which emerge from the first thoracic segment were not interrupted in the second group. The effect of operation in the two groups as judged by the percentage reduction in heart rate was almost identical. This indicates, quite conclusively, that few, if any, cardioaccelerator fibers leave the cord by way of the first thoracic segment.

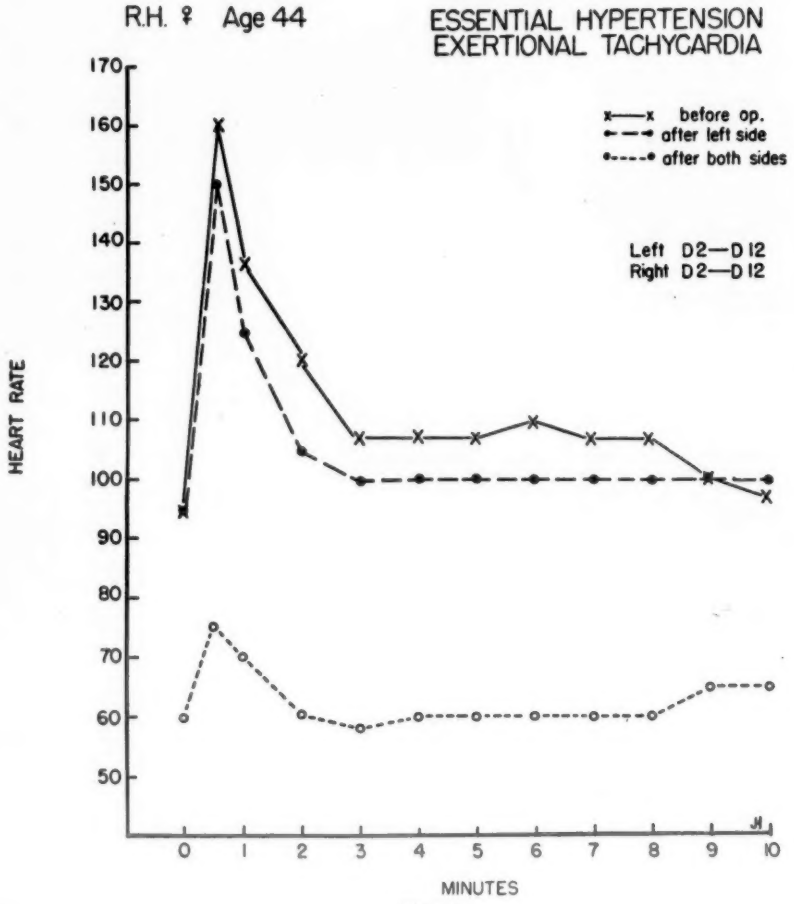

Fig. 4.

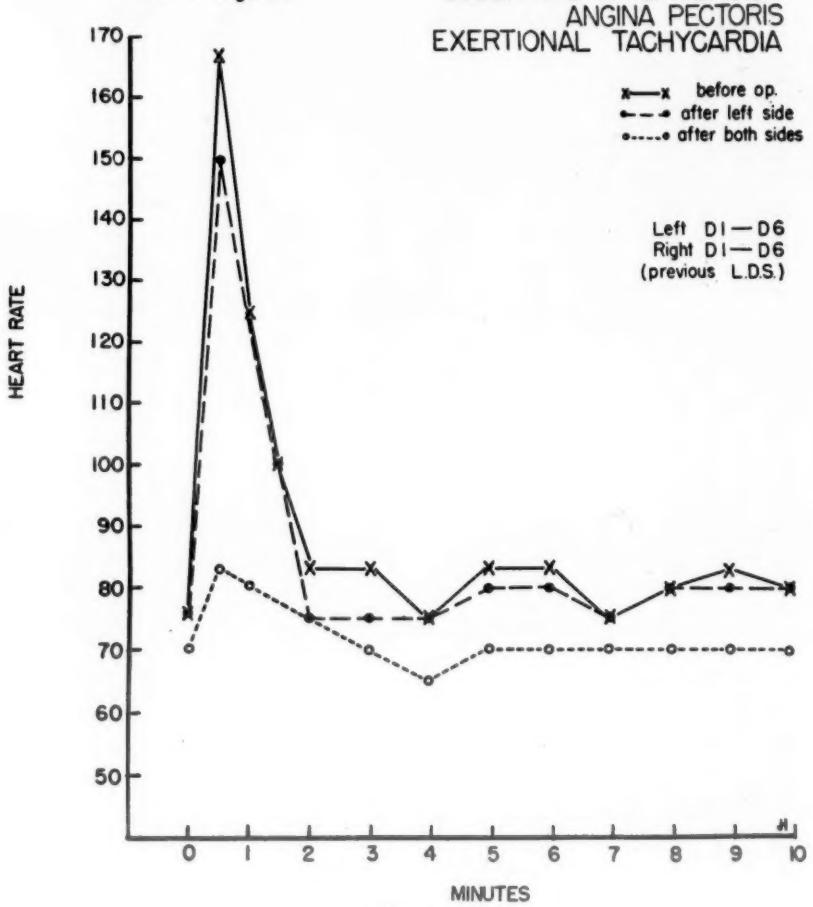

Fig. 5.

Fig. 4.—The exercise test in the case of hypertension and exertional tachycardia.

Fig. 5.—The exercise test in the case of hypertension, angina pectoris, and exertional tachycardia. This case had previous bilateral lumbodorsal splanchnicectomy.

In one case, the sympathetic trunks were removed bilaterally from the third to the eleventh or twelfth thoracic ganglia, inclusive, thus leaving the outflow from the second thoracic segment intact. There was essentially no resultant effect upon heart rate. (See Diagram 3, Fig. 7, and Table I, Group 3.) This indicates that the outflow from the second thoracic segments is of great importance and together with the preceding observations tends to place the upper limit of outflow of cardioaccelerator fibers from the cord at the second thoracic segment. These findings are in keeping with the observations of Kuntz and Morehouse[9] in post-mortem human heart dissections and Saccomanno, Utterback, and Klemme[10] derived from experiments on dogs.

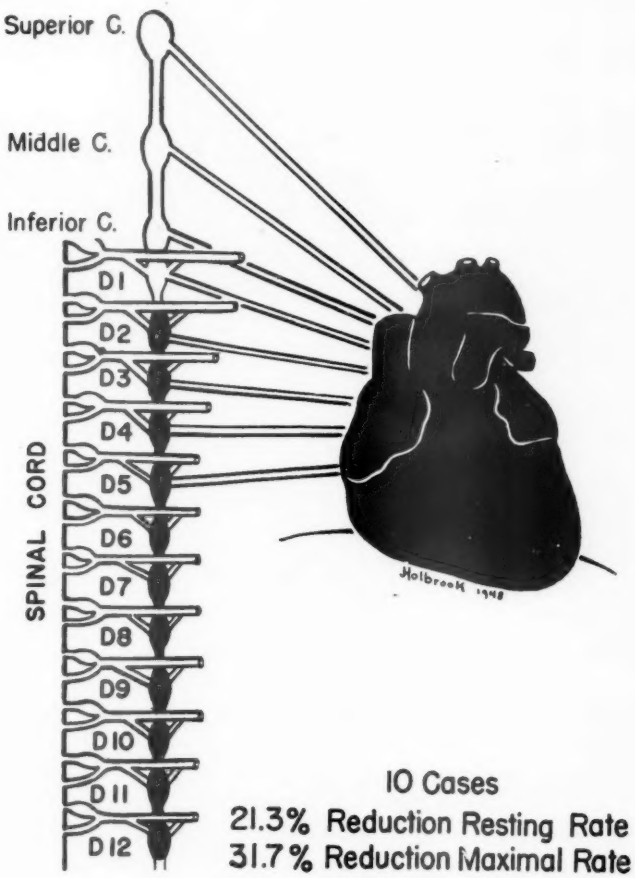

Diagram 2.—Effect of removing D_2 through D_{11} or D_{12} inclusive in ten cases.

Data bearing upon the lower limit of the cardioaccelerator outflow are summarized in Table II. Since it was believed that the first thoracic segment had been excluded from consideration, all operations in which the upper limit of the resection included the second or first thoracic ganglion or the inferior cervical ganglion and in which the lower limit included the sixth to the twelfth thoracic ganglia bilaterally were grouped together. The lower limit was set at the sixth ganglion since direct connections with the human heart have not been described as low as this level. This group (Table II,

Group A) of cases included Groups 1 and 2 in Table I, and in addition six other cases in which the lower limit included the sixth to the ninth ganglia, the upper limits being the same, making a total of twenty-six cases (see Diagram

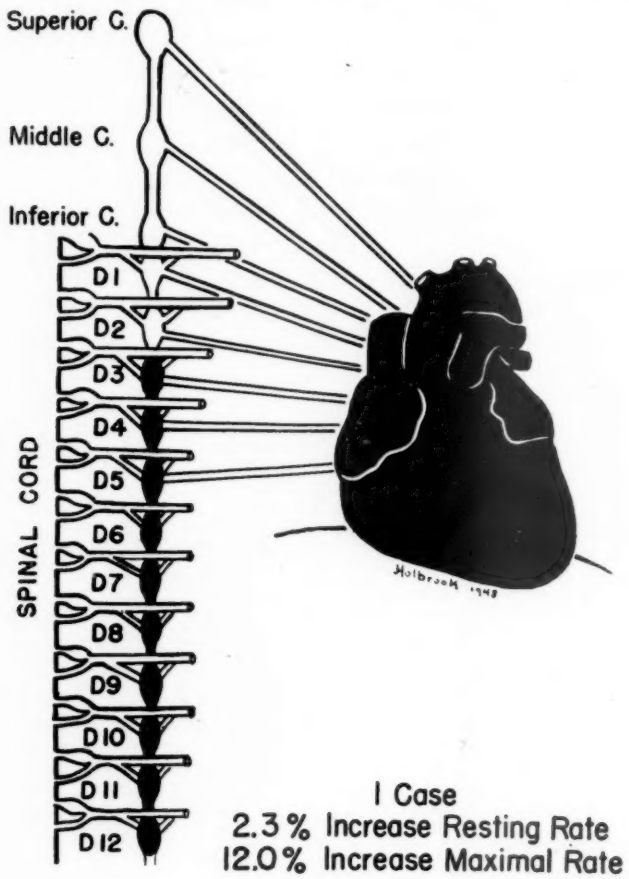

Diagram 3.—Effect of removing the thoracic chain below D_2, bilaterally (see Fig. 7).

4). The effect of operation in these cases is compared with that of lesser resections performed in two smaller groups. The first of these (Table II, Group B) is composed of six cases in which the operative procedures were

TABLE II

GROUP	NO. CASES	OPERATION	EFFECT	RESTING	MAXIMAL.	2 MIN.	5 MIN.	10 MIN.
A	26	Inf. C to T_2 through T_6 to T_{12} inclusive	% Reduction	19.7	33.2	20.8	22.6	21.3
B	6	T_2, T_3, or T_2, T_3, T_4 inclusive	% Reduction	8.3	21.8	5.9	4.4	9.4
C	4	T_2, T_3, T_4, T_5 inclusive	% Reduction	28.9	25.7	31.6	30.9	27.7

The data in this table have to do with the lower level of outflow of cardioaccelerator fibers from the thoracic cord. They indicate that the outflow from the fifth thoracic segment is of consequence and suggest that this is the lower level. All operations were performed bilaterally. The data in Tables I and II suggest that the cardioaccelerator fibers in man emerge from the second to the fifth thoracic segments inclusive.

the equivalent of removing the second and third or the second, third, and fourth thoracic ganglia bilaterally (see Diagram 5). The last group (Table II, Group C) contains four cases in which the sympathetic trunks were removed bilaterally from the second to the fifth thoracic ganglia inclusive (see Diagram 6 and Fig. 6). It will be noted that the effect of operation upon heart rate is marked and probably maximal in Groups A and C, being distinctly less in Group B. This indicates that the outflow from the fourth and fifth thoracic segments is of importance. That the outflow from the third segment is also of consequence can be safely presumed. These findings are consistent with the belief that the lower limit of outflow of cardioaccelerator fibers is the fifth thoracic segment.

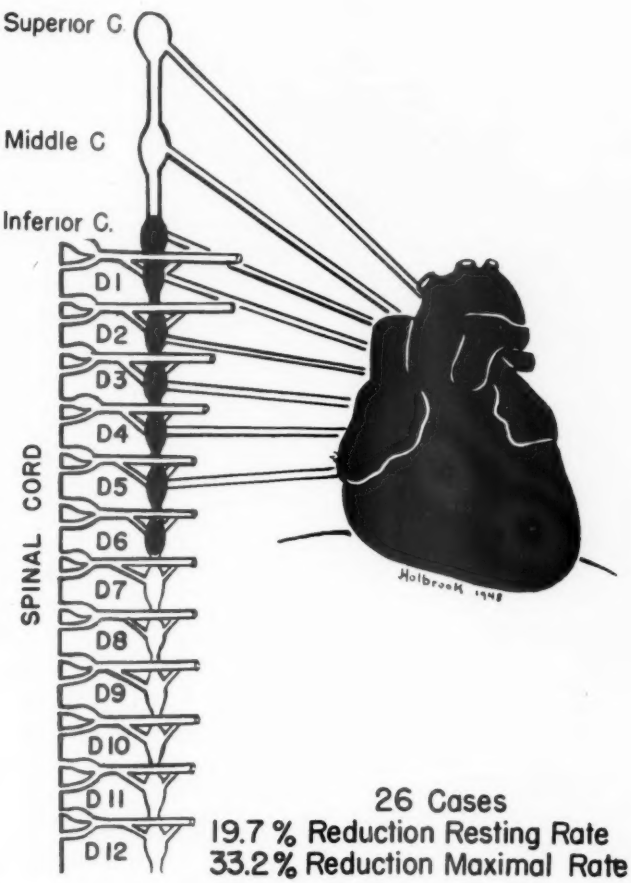

Diagram 4.—Effect of removing inferior cervical to D_2 through D_6 to D_{12} inclusive in twenty-six cases.

EFFECT OF UNILATERAL SYMPATHETIC CARDIAC DENERVATION

It has been apparent from the beginning of this study that complete unilateral sympathetic denervation has only a slight effect upon heart rate. Occasional cases are exceptions to this rule, but if the effect of operation is averaged for all cases having a unilateral denervation it will be found that there is very little change from the preoperative data (Table III). If, however, the

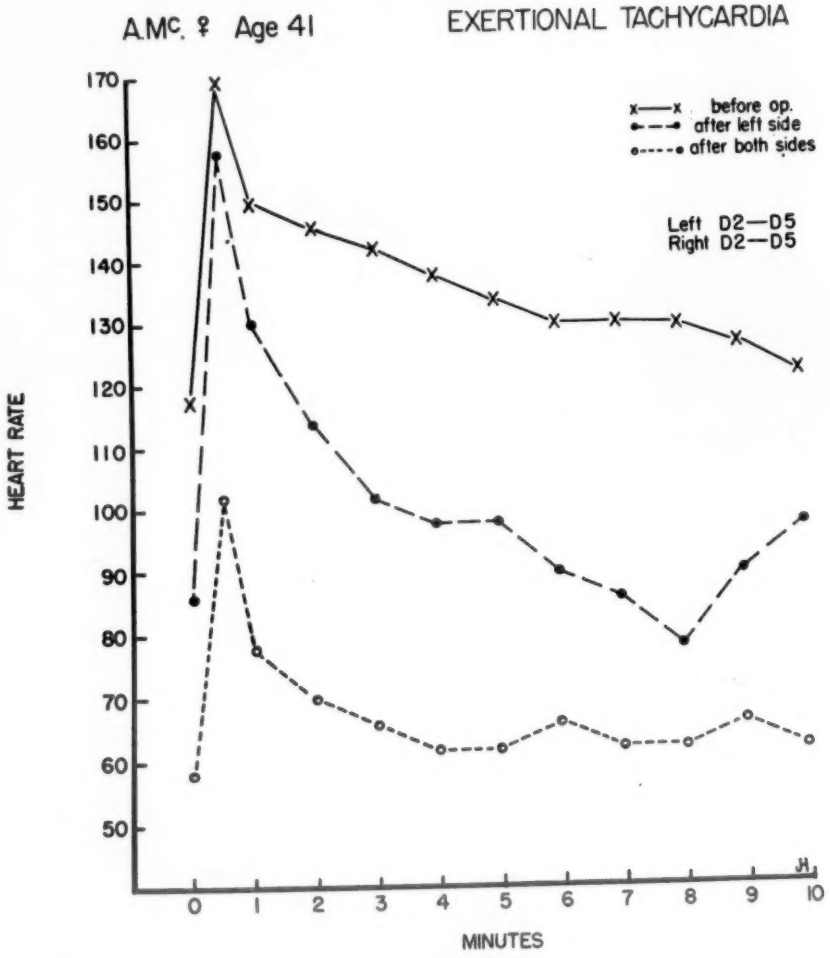

Fig. 6.

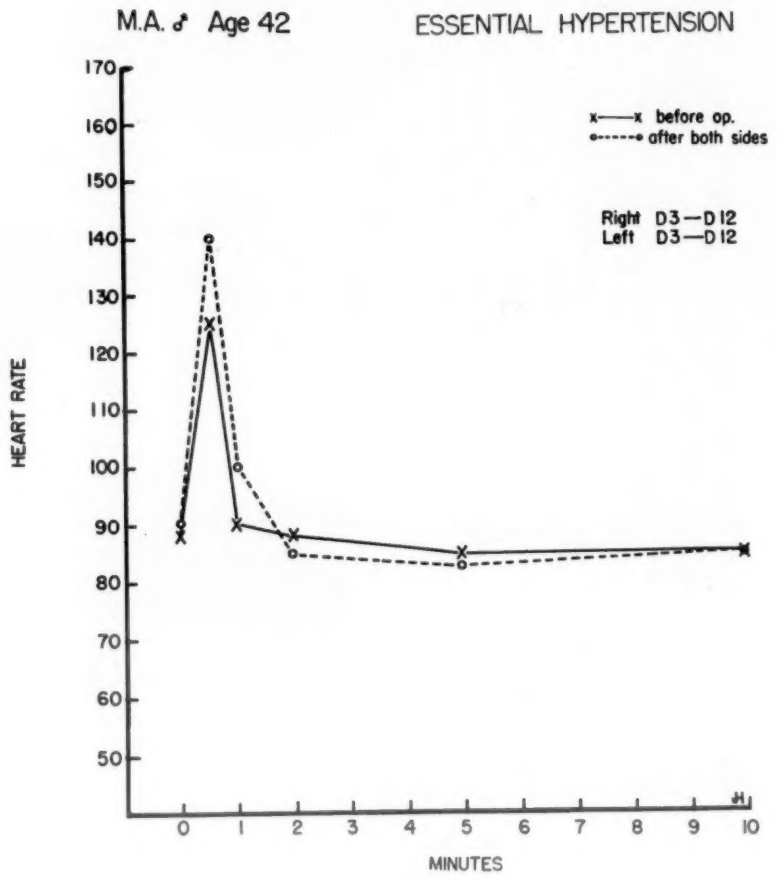

Fig. 7.

Fig. 6.—The exercise test in a case of exertional tachycardia without angina pectoris or hypertension.

Fig. 7.—The exercise test in the previously mentioned case of hypertension in which the second dorsal ganglia were left intact bilaterally (see Diagram 3).

effects of left- and right-sided operations are compared, it is apparent that, in general, right-sided denervations have only a slightly greater effect (Table III). The difference is definite and indicates that the cardioaccelerator outflow from the right side is slightly greater than from the left. The effect of

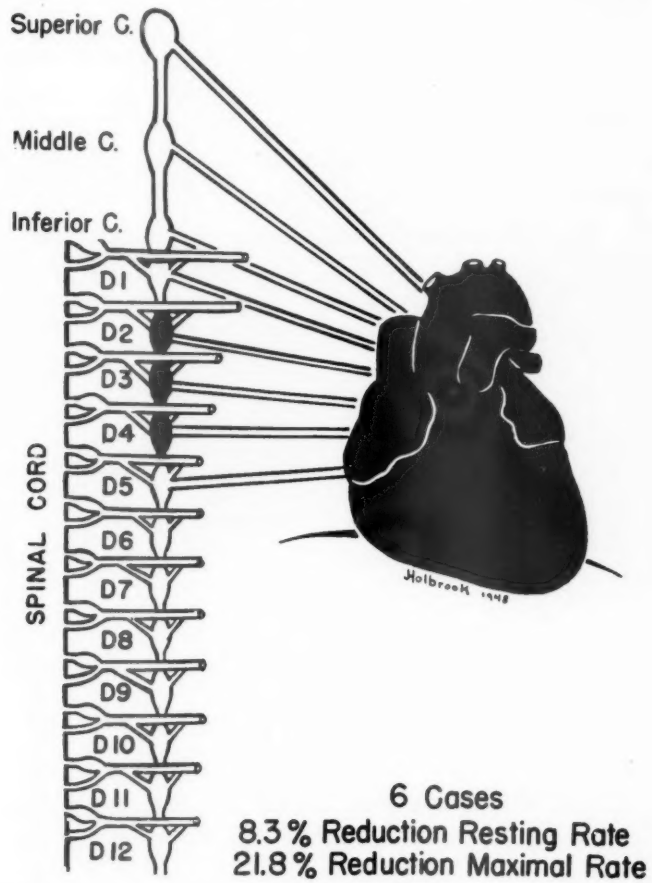

Diagram 5.—Effect of removing D_2 and D_3 or D_2, D_3, and D_4 inclusive in six cases.

TABLE III

OPERATION	NO. CASES	AVERAGE OF PREOPERATIVE RATES					% CHANGE IN RATE POSTOPERATIVELY				
		REST-ING	MAX-IMAL	2 MIN.	5 MIN.	10 MIN.	REST-ING	MAX-IMAL	2 MIN.	5 MIN.	10 MIN.
Unilateral denervation	29	82	128	92	89	90	–1.3	–5.8	–2.1	–3.8	–1.8
Denervation of left side	19	80	129	90	87	88	–0.3	–1.5	+1.9	–0.6	+0.3
Denervation of right side	10	82	127	97	93	90	–1.8	–14.2	–9.3	–9.4	–5.7

In this table the effect of unilateral cardiac denervation without regard to which side had been operated upon is given for twenty-nine cases. The effect was a minimal reduction. In nineteen of these cases, the left side was operated upon first. The effect upon heart rate was less than for the group as a whole, the rates being either slightly slower or faster. In ten cases, the right side was operated upon first. The effect was a slight but definite reduction in all values, particularly in the maximal response to exercise. These data indicate that the right side has a slightly greater effect upon heart rate than the left.

a right-sided denervation is, however, far less than that of a bilateral procedure. It would seem as though a unilateral procedure would probably not be of any practical therapeutic value in the control of rapid heart rates.

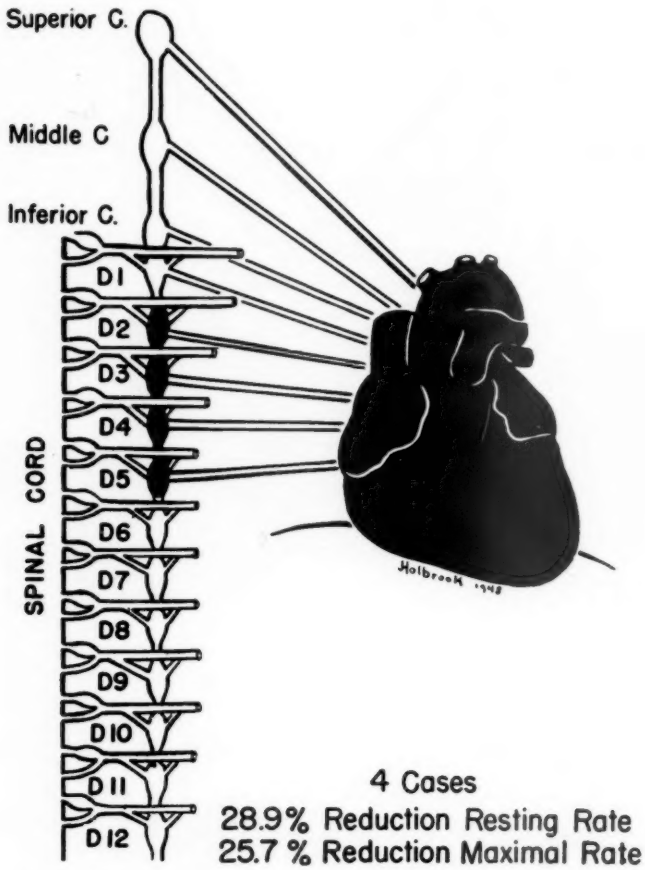

Diagram 6.—Effect of removing D_2, D_3, D_4, and D_5 inclusive in four cases.

THE ROLE OF THE VAGUS AND THE SYMPATHETIC NERVES IN THE CONTROL OF THE HEART RATE

There are many factors which may affect the heart rate. Among these are variations associated with respiration, variations in blood carbon dioxide and oxygen content, variations in body temperature, intracranial pressure, and the quantity of adrenine, sympathin, acetylcholine, thyroxine, and vasopressin which may be in circulation. If we exclude these from this discussion on the presumption that there was no very great alteration of any of these factors in these patients, the effect of operation may be interpreted in terms of vagal and sympathetic activity. Changes in blood pressure are of importance, but in these cases such change was in a direction that would tend to decrease, rather than increase, vagal tone and hence increase heart rate.

With these various factors in mind, the thirty patients having what we believe to be totally sympathectomized hearts were divided into two groups

according to the preoperative resting heart rate. Those with resting rates below 80 were placed in the first, and those with rates of 80 or more in the second. There were fourteen cases in the former (Table IV, Group 1) and sixteen cases in the latter (Table IV, Group 2). It is of interest that the percentage reduction in the pulse rate following operation is several times as great in the faster rate group. This suggests that the faster the resting heart rate, the gretaer is the imbalance between the vagus and the sympathetic. On the other hand, the final pulse rates in the faster rate group are higher than in the slow rate group, suggesting that the increased heart rate might not have been entirely due to increased sympathetic tone but may have been partly due to a decrease in vagal tone. Otherwise the final rates should theoretically have been the same in the two groups. It is also of interest that following sympathectomy there was a decrease in heart rate in the slow rate group. In fact, of the thirty cases under discussion only 3 failed to show a definite slowing of the resting rate after operation. This suggests that the vagus and the sympathetic are both tonically active in man.

TABLE IV

GROUP	PREOPERATIVE RESTING PULSE RANGE	NO. CASES	AVERAGE PREOPERATIVE RESTING RATES	AVERAGE POSTOPERATIVE RESTING RATES	AVERAGE REDUCTION
1	58- 79	14	64	60	7%
2	80-128	16	92	69	25%

The percentage reduction in resting pulse rates after complete cardiac sympathectomy is almost three times as great in the faster pulse rate group (Group 2). The fact that the pulse rate is slower in both groups indicates that tonic sympathetic control of the heart rate exists in man and is from slightly to markedly greater than vagus tone. This imbalance between sympathetic and parasympathetic is greater in the faster pulse rate group, but the fact that the postoperative rates are also faster suggests that in addition to an overactive sympathetic mechanism these may also be a decreased vagus tone.

With regard to the effect of exercise upon the heart rate, it is of interest that the percentage increase in the maximal rate before operation was nearly twice as great in the slow as in the rapid heart rate groups although the maximal rates were higher in the second group (Table V, Groups 1 and 2). After operation, the percentage increase in maximal rate following exercise was exactly the same in the two groups. Such a response is probably mediated by a reflex mechanism in which afferent impulses from the great veins entering the right side of the heart reach the cardiac center by way of the vagus and inhibit vagus tone thus causing an increase in heart rate. The decreased percentage increase in heart rate to the stimulus following operation indicates that a significant portion of the accelerative mechanism in the normally innervated state is due to stimulation of the sympathetic outflow superimposed upon vagus inhibition.

TABLE V

GROUP	PREOPERATIVE RESTING PULSE RANGE	NO. CASES	AVERAGE PREOPERATIVE MAXIMAL RATE	INCREASE ABOVE RESTING RATE	AVERAGE POSTOPERATIVE MAXIMAL RATE	INCREASE ABOVE RESTING RATE
1	58- 79	14	118	85%	81	35%
2	80-128	16	134	46%	93	35%

POSSIBLE CLINICAL APPLICATIONS FOR RESECTION OF CARDIOACCELERATOR FIBERS

The majority of the operations upon which these observations are based were performed for the relief of angina pectoris with (see Fig. 3) or without hypertension. In others, the operations were performed for the relief of vasospasm or hyperhidrosis of the upper extremity. However, in ten cases, hypertension associated with an unusual degree of tachycardia was the reason for including the heart in the denervated area (see Fig. 4). In these cases, the sympathetic trunks were removed bilaterally from the second to the eleventh or twelfth thoracic ganglia, inclusive, in addition to the greater and lesser splanchnic nerves. We have found that in cases of this sort, splanchnicectomy alone may be followed by an increase in tachycardia. In a few cases this has been so distressing that subsequent cardiac denervation has been necessary (see Fig. 5). The early results of near total thoracic sympathectomy in this particular group of hypertensive patients appears to have been helpful.

In four cases, disabling tachycardia, for which no cause other than neurogenic imbalance could be found, was the reason for cardiac denervation (see Fig. 6). In two of these, the resting rates were rapid and rose markedly upon slight exertion. These patients may fall into the category of neurocirculatory asthenia. Both were greatly improved following operation. In the other two cases, the basal rates were higher than normal but the accelerator response to exercise was not remarkable. Both, however, suffered from severe disabling tachycardia upon emotional stimulation, such as meeting strangers or taking examinations. Psychotherapy had been of no avail. Both are greatly improved following operation.

It has been thought that sympathetic motor denervation of the heart might be of help in the management of refractory forms of paroxysmal auricular tachycardia.[15] We have performed cardiac sympathectomy in two such cases. In one case, the first to the sixth thoracic ganglia were removed on both sides. Paroxysmal auricular tachycardia returned some months later although we have no electrocardiographic representation of the attacks in this case. In the second case, in which severe disabling paroxysmal auricular tachycardia occurred in a young woman, denervation was carried out on both sides from the second to fifth thoracic ganglia, inclusive. Attacks recurred following this procedure. The stellate ganglia were removed on both sides at a later operation. The paroxysmal auricular tachycardia again recurred after this procedure. All of these attacks are recorded electrocardiographically. In both of the cases mentioned the recurrent attacks were of marked shorter duration and occurred with much less frequency than before operation and in one case, at the end of two years, the attacks have virtually ceased. This would indicate that cardiac sympathectomy can be effective in certain cases of this type.

SUMMARY

Evidence is presented which suggests that the cardioaccelerator fibers in man arise from the second to the fifth thoracic segments of the cord inclusive and bilaterally.

The outflow from the right side appears to be slightly more important than from the left.

The effect of unilateral cardiac denervation, right or left, upon heart rate is slight by comparison with the effect of bilateral denervation.

Following complete sympathetic motor denervation, the resting pulse rates are slower in all groups, particularly in those having more rapid rates originally. The final rates are faster in the original faster basal rate groups suggesting that tachycardia (resting) is due to a combination of increased sympathetic and decreased vagus tone.

In response to exercise, the percentage increase in maximal heart rate is greater before than after operation, particularly in the slower rate groups. After operation the accelerator response is the same in both groups. This suggests that stimulation of cardioaccelerator fibers is superimposed upon inhibition of vagus tone in causing increased heart rate in response to exercise in the normally innervated state. Following sympathectomy, cardiac acceleration appears to be the result of inhibition of vagus tone.

Resection of the cardioaccelerator fibers in man has been helpful in the management of hypertensive patients having unusual degrees of tachycardia. It has also been helpful in a small group of patients having exertional or emotional tachycardia.

It would appear that cardiac denervation may be an effective procedure in certain cases of paroxysmal auricular tachycardia.

No untoward effects have followed resection of the cardioaccelerator fibers in man, in our experience.

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STAB WOUND OF THE HEART FOLLOWED BY TEMPORARY CESSATION OF THE HEARTBEAT WITH RESUSCITATION BY CARDIAC MASSAGE

A Clinicopathologic Study of One Case of Thirty Days' Survival

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RECORDED cases of cessation of the heartbeat and resuscitation by manual massage are numerous. Barber and Madden,[2, 3] in reviewing the literature up to 1945, gathered 143 cases in which complete recovery was reported in 48. Ordinarily cardiac massage was supplemented by the intracardiac injection of adrenalin. The exact duration of the resulting cerebral anoxia compatible with full recovery has, however, not been established. Barber and Madden estimated the time limit to be five minutes at the most, and more probably between three and four minutes, and they pointed out that reports of successful resuscitation after longer periods of cardiac arrest should be evaluated on the basis of the definition of time interval employed. Since reestablishment of circulation begins the moment manual massage is started, they were of the opinion that the duration of cardiac arrest should be defined as "the time interval between the cessation of the heartbeat and the performance of manual cardiac massage."

Greene[8] reported one case of cardiac standstill of four minutes' duration, occurring during the course of laparotomy. However, in the estimate of duration he included the time taken in massaging the heart and administering artificial respiration, which were instituted simultaneously, but even so, the exact duration of the massage and artificial respiration was not known. If Barber and Madden's definition is adhered to, the period of cardiac standstill was overestimated by Greene. The patient passed the first three weeks after resuscitation in a mentally sluggish state, after which she recovered completely, though retrograde amnesia covering the three-week period persisted.

In another instance, that of Desmarest and Lhermitte,[4] in which the survival period after cardiac massage was somewhat more than forty-eight hours, the cessation of heartbeat was estimated to be of about five minutes. Here also the time spent in massaging the heart and giving artificial respiration was included.

Howkins, McLaughlin, and Daniel[12] presented a case in which during the course of laparotomy the heart stopped beating for an estimated ten or eleven minutes, including seven minutes spent in massaging the heart; tracheal insufflation of oxygen was instituted at the time of cardiac arrest. Eight days

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after resuscitation convulsive seizures occurred. Her muscles were hypertonic, and there were no voluntary or involuntary movements although she responded to painful stimuli. An electrocardiogram done three days before death showed no abnormalities. The patient survived for twenty-six days without regaining consciousness.

Howkins, McLoughlin, and Daniel's case is among the very few in which careful histologic studies have been carried out; therefore, we feel that it is worth while to place on record another instance of temporary cardiac arrest in which survival was sufficiently long to permit the establishment of cerebral changes.

CASE REPORT*

Illness at Time of Admission.—The patient, a 29-year-old colored man, was seated in a bar on the evening of April 20, 1946, when, in an altercation with a friend, he was stabbed in the chest and face with a pocketknife. He walked about one-half a block to a doctor's office where he collapsed. He remained unconscious for an undetermined period of time, and when he awoke he found himself bandaged. He was brought immediately to hospital by ambulance.

Examination.—On admission his pulse was 90 per minute, and blood pressure 105 systolic and 70 diastolic. The site of the wound was in the left third intercostal space, 3.0 cm. left of the sternum. A roentgenogram of the chest failed to reveal anything of note.

Course.—The following day (April 21) the patient's temperature rose to about 100° F. and penicillin therapy, 20,000 units every three hours, was begun. In the afternoon a continuous, aching pain developed in the epigastric region and nausea occurred. The pain was aggravated by coughing. Another roentgenogram failed to reveal effusion in the pericardial or pleural cavities.

Except for a slight elevation in temperature his condition remained satisfactory during the ensuing days. On April 25 roentgenograms taken from the lateral view disclosed a knife blade in the region of the right ventricular wall, which under fluoroscopy was seen to pulsate in unison with the heart. The heart shadow was enlarged, and there was evidence of a small amount of fluid in the pericardial and left pleural cavities.

Emergency operation was scheduled for April 26, and in the meantime the patient's blood pressure and pulse were checked every twenty minutes and were found to be within normal limits. At 3:35 P.M. sodium pentothal-ether anesthesia was started, and about seven minutes later (3:42 P.M.) there was a drop in systolic blood pressure from 110 to 50. The pericardium was aspirated of about 250 c.c. of blood. At 3:55 P.M., during the aspiration, the heartbeat, which was felt against the needle, suddenly stopped. Artificial respiration was begun; owing to collapse of the veins the attempt to inject adrenalin intravenously was unsuccessful. The patient was brought hastily into the adjoining operating room. The chest and pericardium were immediately opened by means of an anterior incision through the left fifth interspace. Clotted and fresh blood was removed from the pericardial sac. The heart was flaccid and in complete arrest. As a consequence of manual massage and injection of 1.0 c.c. of adrenalin into the heart cavity (during which time the patient received oxygen by insufflation), normal cardiac rhythm was restored. The cubital vein was exposed and a transfusion of 2,500 c.c. of blood given. The patient's blood pressure soon returned to normal. The duration of complete cardiac arrest was estimated to have been from three to five minutes.

The operation was continued. The knife blade was found in the base of the right ventricle partially embedded in the sternum. To gain more adequate exposure it was necessary to divide the sternum transversely at the level of the incision. The knife blade, 6.7 cm. in length, was removed and the cardiac wound sutured. The pericardial sac was irrigated with sterile saline solution and left open. After placing 200,000 units of penicillin in the left

*Armed Forces Institute of Pathology Accession 171341.

pleural cavity, the chest was closed and a drain inserted through the seventh interspace in the posterior axillary line. Electrocardiography performed while the patient was still in the operating room disclosed normal cardiac rhythm.

Further Course.—During the ensuing days the patient was in fairly good physical condition but failed to regain consciousness. He reacted only to painful stimuli. Frequent aspirations of the nasopharynx and trachea were necessary. On April 28, generalized convulsive seizures set in and continued intermittently. His legs were rigid and all reflexes hyperactive. His eyes remained open most of the time. Intravenous injections of plasma and glucose-saline solution were given daily. Repeated roentgenograms showed a gradually decreasing cardiac shadow.

The patient's condition remained much the same until about May 21. His temperature, which had remained in the vicinity of 100° F., rose gradually to 105°, the pulse from about 115 to 140, and respirations from about 24 to 40, but the blood pressure stayed within normal limits. He became weaker, lost weight, and a roentgenogram taken May 23 showed mottling of both lung fields. Opisthotonos developed. Death occurred on May 28, thirty days after cardiac arrest.

Laboratory Data.—Blood count on admission to hospital revealed 4,609,000 erythrocytes per cubic millimeter; the lowest value was 3,090,000 on May 15. Leucocytes varied from 12,050 per cubic millimeter on admission to 22,800 on April 30. Urinalysis disclosed albumin and many leucocytes on several occasions. Blood chemistry studies, including estimations of sugar, chlorides, and urea nitrogen, revealed no deviation from normal.

AUTOPSY OBSERVATIONS

Gross Examination.—Post-mortem examination was commenced twelve hours after death. The body was emaciated. The wounds and operative scars were well healed. Both pleural cavities were obliterated by fibrous adhesions. The medial pleural surface was adherent to the pericardium.

The heart, together with the adherent pericardium and pleura, weighed 600 grams. There was a window in the right pericardium which measured 8.5 by 7.0 cm. The healed wound in the right ventricular wall, 2 cm. in length, extended from a point 1.5 cm. beneath the coronary sulcus to 1.0 cm. from the lateral border of the ventricle. On cross section the wound was found to extend almost to the endocardial surface, where grayish-white fibrous tissue, measuring 1.5 mm. in thickness, separated it from the cavity. The endocardial wall in the vicinity of the wound showed rusty discoloration. Continuous with the lateral border of the wound and extending on to the posterior wall of the ventricle there was a partially necrotized area, infiltrated with blood pigment; it measured 3.0 cm. in diameter and occupied the entire thickness of the cardiac wall. The right ventricular wall measured from 4 to 6 mm. in thickness, the left ventricular wall from 12 to 18 mm., the tricuspid ring 12 cm. in circumference, the pulmonic 6.5 cm., the mitral 9 cm., and the aortic 6.5 cm.

The combined weight of the lungs was 1,450 grams. The cut surfaces were dark red and presented raised granular areas, most prominent in the lower lobes, the largest measuring 1.0 cm. in diameter.

The liver weighed 1,500 grams. Except for a few pericapsular fibrous adhesions no changes were observed. The spleen, pancreas, thyroid, adrenals, genitourinary, and gastrointestinal tracts showed nothing remarkable. The kidneys together weighed 350 grams and appeared normal.

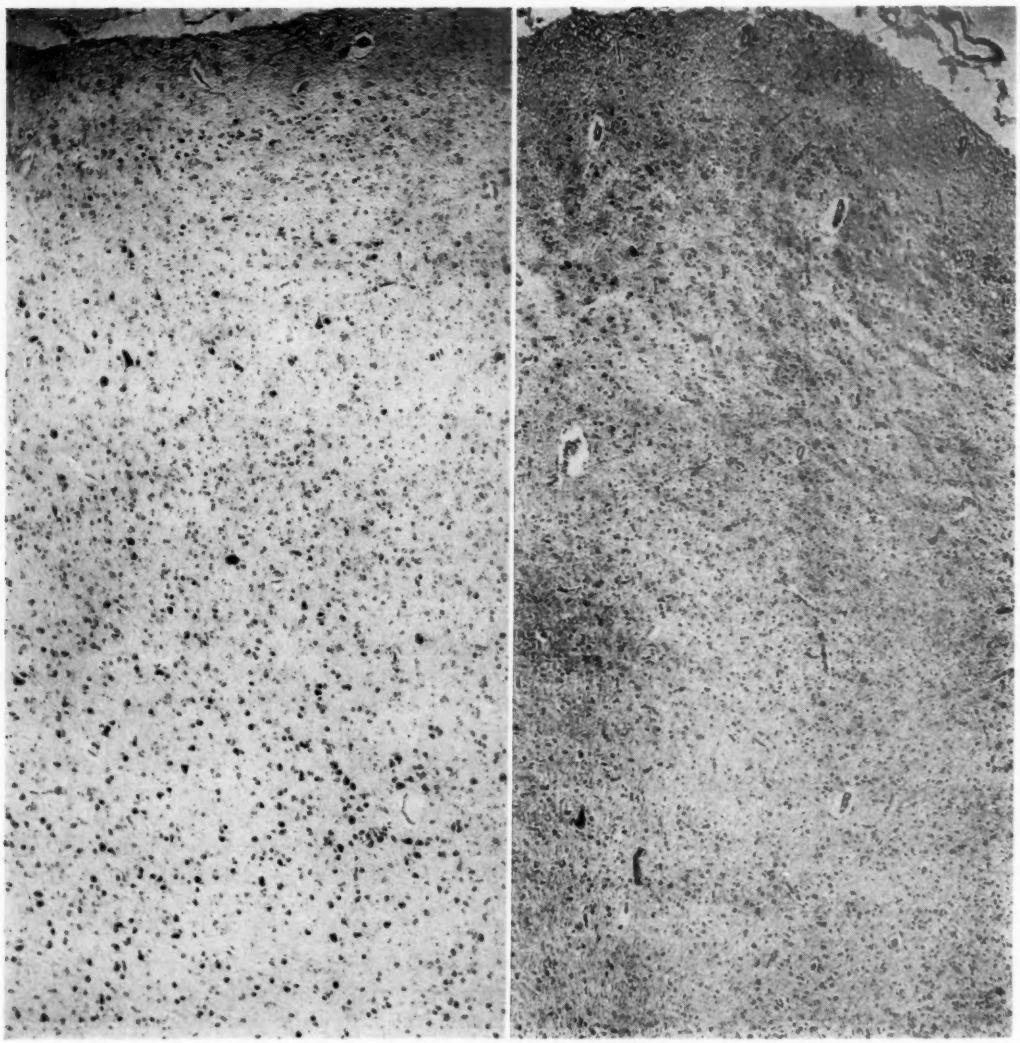
The brain after fixation in formalin weighed 1,600 grams. The external surface appeared normal. On multiple section the only change of note consisted of minute hemorrhages in the lower layers of the cerebral cortex and adjacent white matter in the region of the right superior frontal sulcus at the level of the genu of the corpus callosum, and in the orbital region of the frontal lobe bilaterally.

Microscopic Examination.—

Thoracic and abdominal viscera: Sections removed from the region of the heart wound revealed that healing was well in progress. The heart muscle, brought into apposition by sutures, was joined by scar tissue in which lymphocytes, plasma cells, and a varying number

of pigment-containing macrophages were present. In one section, newly formed cartilage and bone were found in the heart muscle adjacent to the wound. The endocardial tissue displayed fibrous thickening and the endocardial surface was covered by clotted material. Sections from the wall of the heart beneath the posterior leaflet of the tricuspid valve showed necrosis of heart muscle, hemorrhages, and numerous neutrophilic leucocytes. In other sections from the right ventricular wall the interstitial tissue was edematous and contained a few lymphocytes. The epicardium was edematous and fibrous, and contained a moderate number of lymphocytes.

The lungs were the seat of bronchopneumonia. As to the liver, its cells had granular cytoplasm, and some of the nuclei were enlarged and hyperchromatic. No fatty infiltration was present. The spleen, pancreas, kidneys, and adrenal glands showed nothing remarkable.



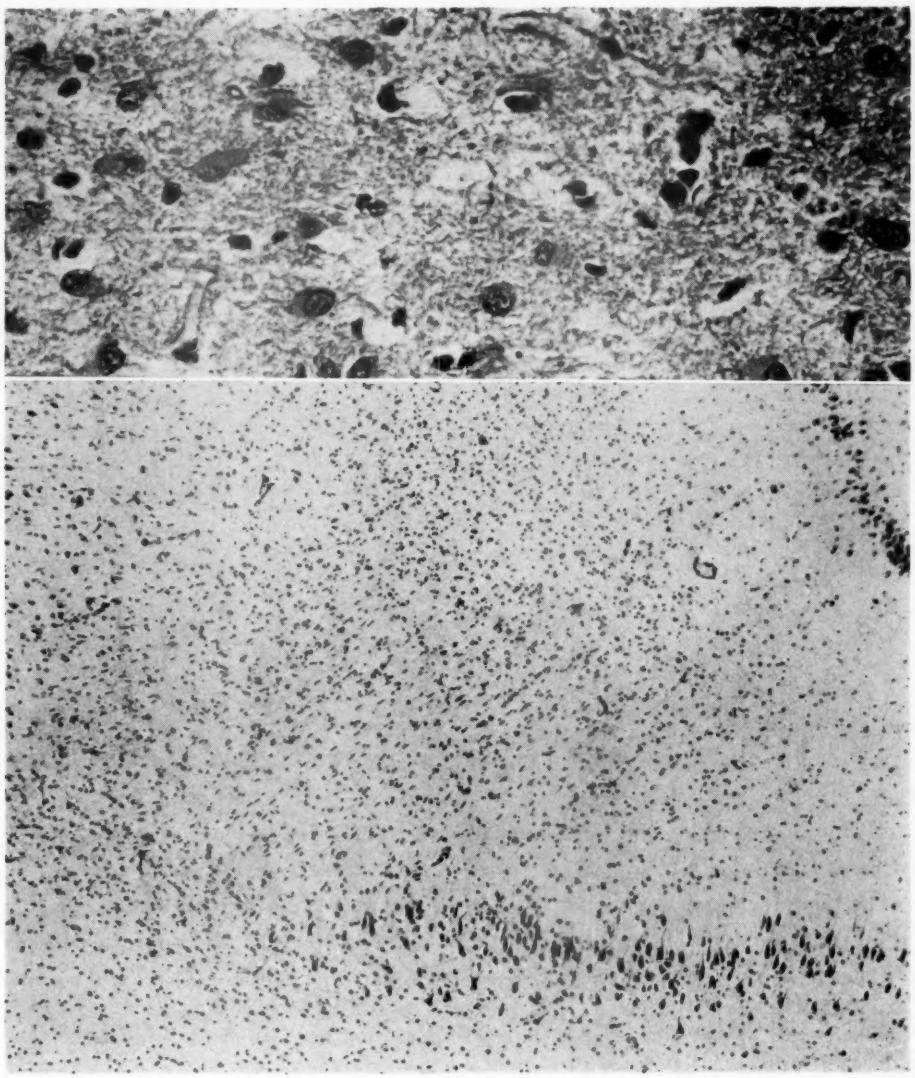
A. *B.*

Fig. 1.—In *A*, from the pericalcarine cortex, there is a general reduction of ganglion cells, with moderate increase in microglia. Most of the ganglion cells in lamina III have disappeared, and many of those in laminae III and V are hyperchromatic (×55). In *B* is illustrated the severe damage inflicted on the calcarine cortex. Lamination has been lost. Lamina III has been converted to a spongy state. Only three or four large ganglion cells are visible (×55, cresyl violet stain).

Brain: Many blocks from the brain, including every gyrus, were removed, so that a study of the topographic distribution of the lesions could be made. The blocks were embedded in paraffin and celloidin, and sections were stained by hematoxylin-eosin, cresyl violet, and by the Weil myelin sheath and the Holzer glia fiber methods. Frozen sections from additional representative blocks were stained by oil red O and by the Hortega method for microglia.

The leptomeninges showed little of note aside from spotty thickening of arachnoidal meshes. Not a single section of cerebral cortex was intact, but the pathologic changes varied in degree in the different areas. Generally there was a diffuse or patchy reduction of nerve cells, with lamina III bearing the brunt of the attack (Fig. 1, *A*). Many remaining nerve cells were shrunken and their nuclei and cytoplasm hyperchromatic. Also there was a dif-

A.

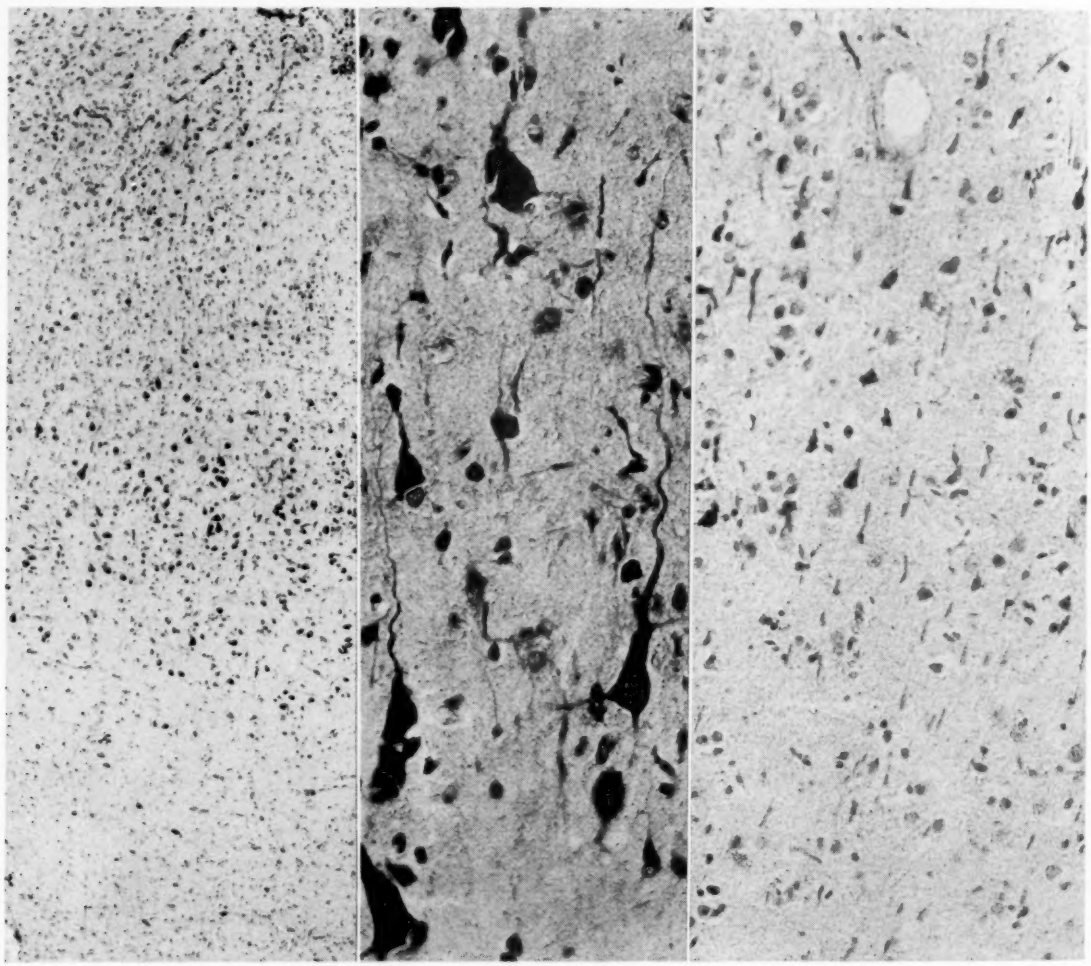


B.

Fig. 2.—In *A*, from lamina III of the calcarine cortex, astrocytes are in great profusion (×400, hematoxylin-eosin stain). In *B* the hippocampus is shown; there is complete disappearance of ganglion cells from Sommer's sector with replacement by swarms of microglia. Scattered proliferated astrocytes also are present. The dentate gyrus (in the upper right corner) is focally degenerated (×62, cresyl violet stain).

fuse proliferation of glial cells, particularly microglial rod cells. In the more severely affected areas astrocytes were numerous. Neuronophagia was occasionally observed.

As mentioned, the pathologic changes were present in all sections, but in the calcarine and adjacent cortex (areas 17, 18, and part of 19, of Brodmann) they were particularly conspicuous. In area 17 there was a relatively large area bilaterally (about 1.0 cm. of cortex on each side) in which the laminae were largely replaced by proliferated glia (Fig. 1, *B*),



A. *B.* *C.*

Fig. 3.—A, Medial frontal gyrus, illustrating diffuse dropping out of ganglion cells, with replacement by myriad microglia (×62). *B*, From the same gyrus, showing hyperchromatic ganglion cells, with corkscrew-like deformation of apical dendrites and scattered microglia (×275, cresyl violet stain). In *C*, from the same gyrus, and stained by oil red O, fat is visible in the processes of some of the microglia and in the few remaining ganglion cells (×160).

mainly swollen astrocytes (Fig. 2, *A*), and microglia. Furthermore, Sommer's sector of the hippocampus was severely damaged, only a few nerve cells remaining; rod cells and astrocytes were in great profusion (Fig. 2, *B*). The dentate gyrus also showed foci of degeneration (Fig. 2, *B*). As to vessels in the cerebral cortex, slight vascular engorgement was noted, but there was no endothelial or adventitial proliferation. Edema was inconspicuous. Corresponding to the hemorrhagic areas in the frontal lobes noted on gross inspection, there were a number of dilated and engorged vessels, but no hemorrhages. These vessels probably were preexistent venous malformations. The cortex adjacent to these vessels showed changes similar to those in the calcarine area, except that they were less severe (Fig. 3, *A*). As elsewhere,

many remaining nerve cells showed degenerative changes, including corkscrewlike deformation of apical dendrites (Fig. 3, *B*). Oil red O stained sections showed fat in moderate numbers of microglia and in many of the remaining nerve cells (Fig. 3, *C*), a finding most striking in Sommer's sector of the hippocampus.

The subcortical white matter displayed only a generalized slight to moderate increase in oligodendroglia and a scattering of rod cells; no demyelination was observed. The same minor changes were apparent in the corpus callosum, the anterior and posterior commissures, the optic tracts, and the internal capsule. On the other hand, the intrahypothalamic part of the fornix showed a pronounced proliferation of oligodendroglia. The subependymal cell plate contained patchy accumulations of microglial cells, generally arranged parallel to the ventricular wall. The ependymal lining of the ventricles was intact except for occasional small granulations of the wall of the third ventricle. A few vessels of the choroid plexuses were fibrous and thickened.

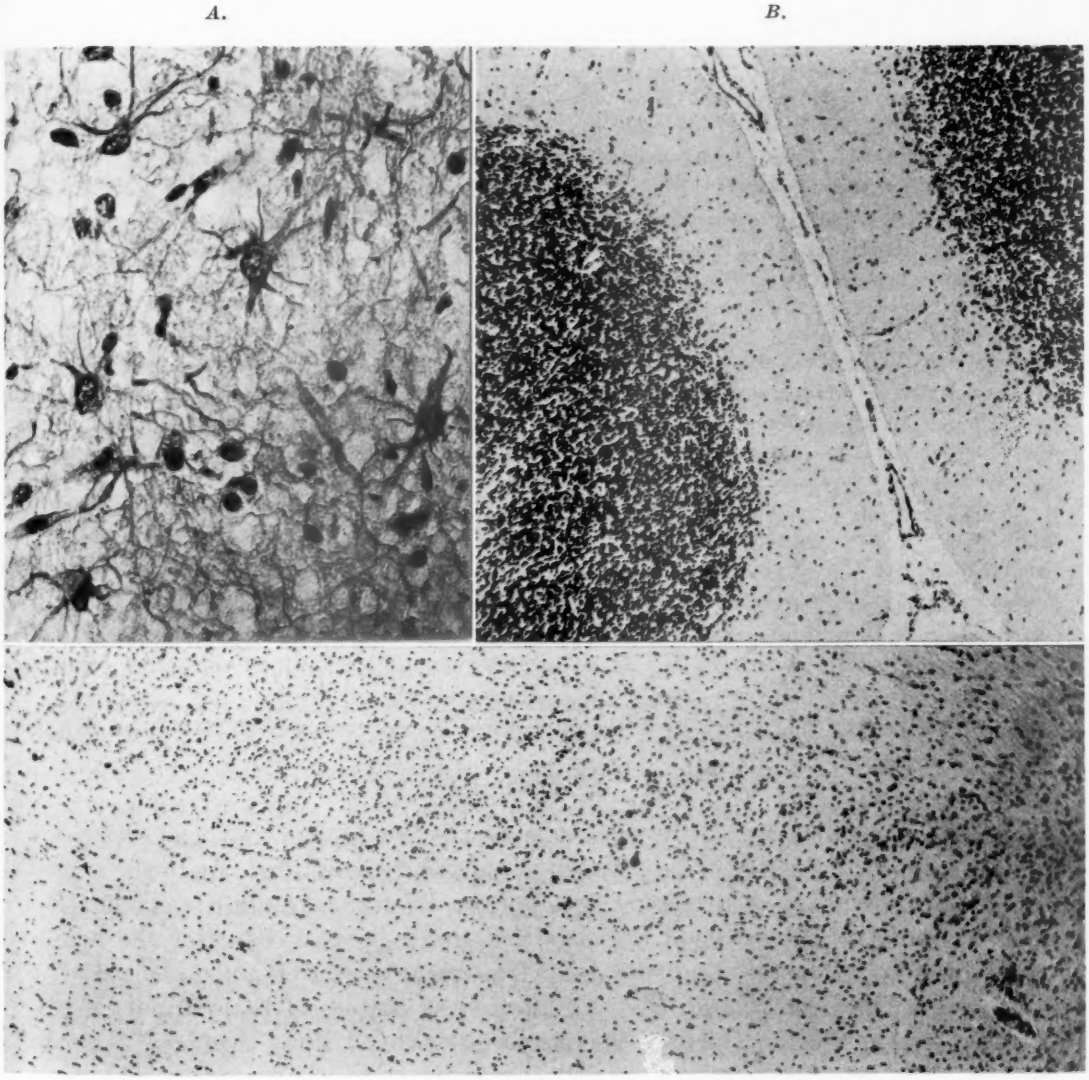


Fig. 4.—*A*, From the pulvinar of the thalamus, showing conversion of parenchyma into spongy state, with proliferation of astrocytes (×250, Holzer stain). In *B*, from cerebellar folia, all Purkinje cells have disappeared, and cells of the Bergmann layer have increased in number (×100). In *C*, from the dentate nucleus, very few ganglion cells remain, and there is diffuse microglial replacement (×90, cresyl violet stain).

Examination of sections from the basal ganglia disclosed that the most striking changes were in the thalamus. All the thalamic nuclei were equally affected except those most ventrally situated, which were virtually free from change. Many nerve cells had been replaced by a loose glial scar (Fig. 4, *A*), and numerous remaining nerve cells showed evidence of disintegration. Satellitosis and neuronophagia were occasionally observed, and there were scattered *gliarasen*. Vessels showed hyaline or fibrous thickening of adventitia, and some were calcified and surrounded by glial scar tissue in which calcified bodies were scattered; in the perivascular spaces and parenchyma there were occasional minute hemorrhages and a few large mononuclear cells and macrophages. In the caudate nucleus and putamen there was also severe loss of nerve cells with corresponding proliferation of rod cells and astrocytes. Scattered satellitosis was present, and there were many *gliarasen*. The globus pallidus was much less severely affected. The claustrum displayed a moderate loss of nerve cells and sparse proliferation of rod cells.

In sections from the substantia perforata anterior and amygdala little alteration of nerve cells and only slight proliferation of microglia were observed. The nucleus basalis was intact except for scattered rod cells and occasional neuronophagia. In the hypothalamus a few nerve cells were pyknotic; there was considerable microgliosis of the nuclei tuberis laterales, slight proliferation of microglia in the supraoptic, ventromedial, and posterior hypothalamic nuclei, and in the mammillary bodies, and only occasional microglia in the lateral hypothalamic nucleus.

The medial geniculate body showed considerable loss of nerve cells and a corresponding increase in microglia and astrocytes, to almost the same degree, in fact, as the thalamus. The lateral geniculate body was somewhat less affected. The substantia nigra and basis pedunculi were virtually intact. In the red nucleus and superior colliculi, scattered neuronophagia was observed, and a slight to moderate number of nerve cells displayed ischemic changes. Occasional cells of the oculomotor and trochlear nuclei were shrunken, while a few others were swollen and had peripherally displaced nuclei. Occasional microglial cells were seen. The nuclei of the basis pontis had somewhat less than the usual complement of nerve cells, and there was slight focal and diffuse increase in glia. The remaining pontile nuclei were relatively normal except for apparent ischemic changes.

The medulla oblongata showed a slight diffuse proliferation of oligodendroglia and microglia. A few small perivascular hemorrhages were present in the floor of the fourth ventricle.

The sections from the cerebellum exhibited almost complete loss of Purkinje cells and moderate proliferation of cells of the Bergmann layer (Fig. 4, *B*). The dentate nucleus displayed severe loss of nerve cells and replacement by countless glia of all categories, particularly microglia (Fig. 4, *C*).

Spinal cord: One section from the uppermost cervical cord showed nothing of significance.

DISCUSSION

The exact duration of the cardiac arrest is not known, but was estimated by the attending surgeon to be between three and five minutes. As to the period of cerebral hypoxia, it doubtless was longer if one takes into consideration the preliminary fall in blood pressure and the time required after the beginning of manual massage of the heart for complete re-establishment of the circulation; however, these may be regarded as factors of little import if one accepts the conclusion of Hill[11] that a mere trickle of blood through the brain serves to maintain life in nerve cells. From the data in our case, which were very similar to those of Howkins, McLaughlin, and Daniel[12] as regards time interval, symptoms and histologic findings, it would seem that the maximum period of cardiac arrest compatible with full recovery is less than five minutes.

The most striking symptom in our case was permanent unconsciousness, and, as might be expected, the cerebral cortex was severely damaged. The whole of the calcarine cortex, patchy areas in the middle frontal gyrus, and Sommer's sector of the hippocampus bore the brunt of the attack. All other parts of the cortex were also affected, and to about an equal degree, except for the precentral gyri which were somewhat more affected than contiguous parts of the frontal and parietal lobes.

The striking vulnerability of cerebral cortex in stagnant anoxia has been well established in experimental animals, as Grenell[9] has brought out in his recent review of the subject. Following occlusion of the pulmonary arteries of cats for varying periods of time, Weinberger, Gibbon, and Gibbon[14] found no adverse effects if circulatory arrest lasted no longer than three minutes and ten seconds, but if the period was longer the animals exhibited loss of vision, motor disturbances, abnormal behavior, and stupor; laminae III and IV of the cortex were the most affected. Impaired vision and hearing were noted by Windle and Becker[15] in guinea pigs in which asphyxia neonatorum had been produced by temporarily clamping the umbilical cords in late fetal life, but histologic examination of the brains failed to reveal a prevalence of lesions in the visual cortex. Gildea and Cobb[5] occluded the vertebral and the subclavian arteries in cats for varying periods of time, and found devastated cortical areas in which the pyramidal cells in laminae V seemed most affected. In similar experiments in cats, Gomez and Pike[7] observed that the small pyramidal cells of the cortex were the most sensitive, but they did not mention relative laminar vulnerability. Furthermore, Grenell[9] observed in dogs in which the cerebral circulation was completely arrested by means of a cervical pressure cuff (after preliminary removal of the spine and laminae of the second cervical vertebra so that the vertebral and spinal arteries could be compressed) that damage to cortical nerve cells, particularly in laminae III and IV, occurred in as short a time as two minutes after circulatory arrest. In our case, pyramidal cells in laminae III suffered most, except in the precentral gyrus where large Betz cells had also disappeared. The most devastated area in the brain was the calcarine cortex (area 17 of Brodmann) where only laminae I, II, and VI could still be recognized. This was true also in the case reported by Howkins, McLaughlin, and Daniel,[12] who remarked that, "The findings of many investigators have been that the occipital cortex suffers severely and early in cerebral anoxia." Desmarest and Lhermitte[4] also noted in their case of somewhat more than forty-eight hours' survival that the visual cortex was severely affected. In Nielsen and Sanborn's case, damage to the occipital lobe was restricted to areas 18 and 19 unilaterally. In this connection it may be mentioned that visual disturbances may be encountered in nonfatal cases of anoxia. Baker[1] referred to two cases in this category: One concerned a 4-year-old boy who during appendectomy suffered a sudden cardiac and respiratory arrest for "several minutes," but was revived by the intracardiac administration of adrenalin. Postoperatively he was blind, but as time went on, a moderate degree of vision was restored. The other instance

was that of a 4-year-old girl who, during operation for Pecquet's ductus, had cardiac arrest for eight minutes. During the ensuing three weeks she was completely blind, but five weeks later she could see very large objects enough to avoid them, but could not recognize them as such. Months later the visual disturbance was still severe.

The advanced destruction of the thalamus and striatum was in conformity with the observations of Howkins and associates, though Desmarest and Lhermitte[4] found that of the two structures, the thalamus was most affected. The globus pallidus, on the other hand, was little involved, as is often the case in stagnant anoxia.

Another severely affected part of the brain was the cerebellum, particularly the dentate nucleus. The observation that many Purkinje cells had disappeared is in accord with the findings of Howkins and co-workers, Gomez and Pike,[7] Weinberger, Gibbon, and Gibbon,[14] and Grenell,[9] and at variance with that of Windle, Becker, and Weil,[16] who presented evidence that Purkinje cells have a remarkable recuperative capacity. As to the hypothalamus, its nerve cells were intact although some displayed ischemic changes, and in some nuclei there were proliferated microglia. Such an observation is in line with the acknowledged relative immunity of the hypothalamus to anoxic insult, even the histotoxic anoxia produced by cyanide (Ginzler and associates[6]), though Grenell and Kabat[10] noted severe damage to hypothalamic nuclei (supraoptic, paraventricular, and lateral mammillary nuclei excluded) in dogs subjected to cerebral circulatory arrest for nineteen minutes or more.

In attempting to assess the comparative severity of the lesions in the central nervous system as a whole, the following conclusions were reached: damage was *severe* in the cerebral cortex (especially the calcarine area), thalamus (except its ventral part), striatum, cerebellum, and medial geniculate body, *moderate* in the lateral geniculate body, *mild* in the globus pallidus, claustrum, hypothalamus, and red nucleus, and *virtually absent* in the substantia perforata anterior, amygdala, subthalamus, substantia nigra, pons, medulla oblongata, and uppermost spinal cord. The white matter as a whole was well preserved.

Of especial interest were the countless microglia pervading the cerebrum even in areas in which little cell damage could be detected. It seemed that the microglial response was out of proportion to the degree of nerve cell damage. Comparable in this respect was the observation of Windle, Becker, and Weil[16] in the guinea pigs already referred to, that swarms of microglia appeared 2½ days after asphyxiation, emerging from the ependymal region of the lateral recess of the fourth ventricle and the anterior horns of the lateral ventricles. At the end of one week they had invaded diffusely and indiscriminately the entire brain, and after three to four weeks had disappeared. In our case no evidence as to their origin could be found, although they were fairly numerous in certain parts of the subependymal cell plate.

The precipitating cause of death in our case was regarded as pneumonia. Throughout the course the heart showed no evidence of decompensation, al-

though sinus tachycardia persisted. Histologic examination of the heart revealed that healing was well in progress.

SUMMARY

A man stabbed in the heart was found six days later to have pericardial hemorrhage. During pericentesis the heart stopped beating. The pericardial cavity was hastily opened, the heart massaged, and adrenalin injected, whereupon the heart began again to beat. It is estimated that the cardiac arrest lasted from three to five minutes. The patient survived for thirty days thereafter, the longest thus far recorded in such cases. He remained unconscious during the entire time.

Post-mortem examination disclosed severe changes in the brain, which consisted mainly of disappearance and degeneration of ganglion cells and replacement by myriad microglia and a smaller number of astrocytes. The cerebral cortex was a site of predilection, with the calcarine cortex bearing the brunt of the attack, an observation which bears re-emphasis in view of the potential visual disturbance after nonfatal anoxia. Other severely affected structures were Sommer's sector of the hippocampus, thalamus, striatum, cerebellum, and medial geniculate body. The white matter of the cerebrum was virtually spared.

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TENSION ON THE SUTURE LINE IN PERIPHERAL NERVE SURGERY

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THE maxim that tension shall not be placed on the suture line in a neurorrhaphy has been generally accepted. This follows the general principle of surgery that sutures shall be placed without tension wherever possible. That serious consequences will follow the use of tension in neurorrhaphy has been stated unequivocally, or implied indirectly, by many authors.[1-4] In contradistinction, Frazier[5] and Sanders[6] considered that slight tension was not certainly harmful. Whether suture without tension is or is not desirable, its performance is frequently extremely difficult or even impossible with the large nerve gaps resulting from the wounds of modern war or industrial and traffic accidents. Even with the methods of nerve transplantation and joint positioning at our disposal, it is frequently impossible to approximate the nerve ends without tension.[7] The results of the massive dissections or bone resections for extremity shortening to obtain nerve length[8] may be as disabling as the nerve injury itself.[9] Staged procedures, if properly utilized, result in a decrease in the ultimate tension. Since nerve grafts for the large major nerves have in general given unsatisfactory results,[10, 11] although more recently Seddon[12] and Holmes[13] have indicated that better results may be expected, the most satisfactory method for obtaining re-innervation remains nerve suture with or without tension.

The purpose of the present study was to determine the effects of tension applied to the suture line on the end results of neurorrhaphies in a small group of carefully observed cases. Three hundred three cases, or approximately one-fifth of the major neurorrhaphies studied, had the necessary information for proper evaluation (Table I). All cases were studied at Wakeman General Hospital and most patients were operated upon at that hospital, although cases were included from almost all Army neurosurgical centers.

RESULTS

The 303 cases were divided into two groups. Group 1 includes all those cases followed long enough to observe a final definitive result. Group 2 includes those in which a definitive result could not be established because of: (1) insufficient follow-up, (2) severe associated injuries, especially to bones, joints, or muscles, and (3) preoperative function not commensurate with the obvious nerve lesion.[14]

When the cases with definitive results (Group 1) are evaluated (Table II), it becomes apparent that in this group the nerves which were repaired under slight to moderate tension had the most satisfactory final results. As might be expected, none of the nerves sutured with maximum tension had a complete return of function, but many had fair and good results (85.6 per cent). Even

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TABLE I. TOTAL NUMBER OF CASES OF EACH NERVE AND NUMBER OF CASES FOR EACH TENSION GROUP*

NERVE	NUMBER OF CASES	PER CENT OF TOTAL CASES	NUMBER WITH TENSION OF 0	1	2	3	4
Median	52	17.0	12	9	18	10	3
Ulnar	105	34.7	29	18	34	20	4
Radial	51	16.8	10	9	16	12	4
Brachial plexus	6	3					
Musculocutaneous	1		0	4	1	3	1
Axillary	2						
Sciatic	43	14.1	4	7	13	14	5
Tibial	19	6.3	2	2	5	6	4
Peroneal	24	7.9	2	5	7	9	1
Total cases	303		59	54	94	74	22

*The musculocutaneous and axillary nerves are included with the brachial plexus for the breakdown by tension. In this and all subsequent tables the tension is indicated by figures 0-4, as follows:

0 indicates ends in approximation with nerves lax;
1 indicates a minimum tension necessary to approximate the ends;
2 indicates a moderate tension necessary to approximate the ends;
3 indicates a marked tension necessary to approximate the ends;
4 indicates the maximum tension the nerve will stand without tearing, necessary to approximate the ends.

In two instances (Cases 1 and 2) even with this maximum tension it was impossible to approximate the ends.

TABLE II. CASES WITH DEFINITIVE RETURN OF FUNCTION*

DEGREE OF RETURN OF FUNCTION	DEGREE OF TENSION 0 NO. OF CASES	0 PER CENT	1 NO. OF CASES	1 PER CENT	2 NO. OF CASES	2 PER CENT	3 NO. OF CASES	3 PER CENT	4 NO. OF CASES	4 PER CENT
4 Excellent	3	7.7	5	14.3	12	18.1	7	21.2	0	0
3 Good	12	30.7	22	62.8	23	34.8	14	42.4	6	42.8
2 Fair	12	30.7	5	14.3	17	25.7	9	27.2	6	42.8
1 Poor	8	20.5	2	5.7	11	16.6	2	6.0	1	7.2
0 No return	4	10.3	1	2.9	3	4.5	1	3.0	1	7.2

*Return of function in the vertical scale is rated as 0, 1, 2, 3, 4. 0 indicates no return of function; 1 indicates return of one element either motor or sensory; 2 indicates return of function from one element to 50 per cent of the total innervated elements; 3 indicates return of function from 50 per cent to all but one innervated element; and 4 indicates return of function of all elements. Tension, as in all tables, is on the horizontal scale. Percentages are based on the total number of cases in each tension group.

TABLE III. CASES WITHOUT DEFINITIVE RETURN OF FUNCTION (GROUP 2)*

ESTIMATION OF RETURN OF FUNCTION	DEGREE OF TENSION 0 NO. OF CASES	0 PER CENT	1 NO. OF CASES	1 PER CENT	2 NO. OF CASES	2 PER CENT	3 NO. OF CASES	3 PER CENT	4 NO. OF CASES	4 PER CENT
Return of function	49	83.0	52	96.3	84	89.3	63	85.1	19	86.3
No return of function	5	8.5	1	2.0	7	7.4	3	4.0	3	13.7
Advance of Tinel sign	43	73	44	81.5	55	58.5	50	67.5	19	86.3
No advance of Tinel sign	3	5	2	3.7	6	6.4	2	2.7	1	4.6

*The percentages are on the basis of all cases in each group.

in cases where it was impossible to approximate the nerve ends by the use of maximum tension, satisfactory results have been obtained as in Case 1.

CASE 1.—C. B., a soldier, had a neurorrhaphy of the radial nerve at the mid one-third of the humerus on March 28, 1945, six months after injury. A large neuroma was excised to reach fair nerve ends. Even with marked tension it was impossible to bring the nerve ends into apposition, and a gap of approximately 3 mm. remained at closure. By six months after operation there was return of function of the brachioradialis and supinator muscles and a Tinel sign to 20 cm. Despite this return of function, and because of the supposedly unsatisfactory neurorrhaphy, the nerve was re-explored on Oct. 2, 1945. A fairly large, irregular neuroma, 2 cm. in length, was found at the suture site (Fig. 1). Stimulation of the nerve both above and below the suture line gave contraction of the brachioradialis, supinator, extensor carpi radialis, and extensor carpi ulnaris muscles. A partial external neurolysis was performed. By the time of discharge, three months after operation, there was good voluntary contraction of these muscles, plus beginning function of the abductor pollicis longus and extensor pollicis longus, and there was beginning return of sensation.

Fig. 1 (Case 1).—Photograph at reoperation of the radial nerve sutured under tension of 4 with a gap of approximately 3 mm. Shown partially dissected.

It is surprising to find that the nerves sutured without any tension actually gave the poorest results in this series, having the lowest percentage of excellent and good results, 38.4 per cent as compared with 71.1 per cent, 52.9 per cent, 53.6 per cent, and 42.8 per cent, and the highest percentage of poor results and no return of function, 30.8 per cent as compared to 8.6 per cent, 21.1 per cent, 9.0 per cent, and 14.4 per cent.

The cases in Group 2 were rated only as showing some return of function, or advance of the Tinel's sign. There is no significant difference in the percentage of cases showing return of function or advance of the Tinel sign in the various tension groups. However, again the nerves repaired without tension had the lowest percentage of return of function (Table III).

The number of cases in which reoperation was deemed necessary and the findings at reoperation are of some importance in evaluating results following neurorrhaphy (Table IV). All cases with reoperation are briefly reviewed (Table V). In cases with marked tension there was a definite tendency to re-explore early because of the prevailing opinion that with tension failure was assured. In many cases, re-exploration was performed as an incidental procedure at the time of operation on other nerves as in Cases 9, 24, and 25, and in other cases only because of the presence of a trigger point, as in Cases 11 and 17.

TABLE IV. CASES WITH REOPERATION AND NUMBER OF CASES WITH VARIOUS TYPES OF PATHOLOGY IN EACH TENSION GROUP*

	DEGREE OF TENSION									
	0		1		2		3		4	
RESULTS OF OPERATION	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT
Reoperated	6	10.1	5	9.2	8	8.5	7	9.4	5	22.7
Separation of the suture line	1	1.7	1	1.8	0	0	2	2.7	2	9.0
Large neuroma	2		2		2		0		1	
Small neuroma	1		1		2		2		2	
Scarring	2		0		1		1		0	
Normal appearance	0		1		3		2		0	

*The percentages are computed from the total number of cases in each tension group.

The actual condition of the nerves at reoperation is of significance. As might be expected, there were relatively more cases with separation of the suture line in the groups with high tension. However, even in the group with maximum tension, this number is not extreme (two cases, or 9 per cent). It is of interest that all separations occurred in those cases repaired with simple epineural sutures regardless of the type or size of suture material, except in two cases in which the type of suture was not stated (Cases 2, 3, 7, 12, 20, and 27). There was no instance of suture line separation in those cases known to have been repaired with stay sutures in the sheath. (See discussion.)

All but one of the separations occurred in the peroneal nerve or the peroneal segment of the sciatic nerve (Cases 2, 3, 7, and 27). The remaining case was a partial separation of the median nerve (Case 20).

The presence of neuromas and scarring in the nerve was also recorded. The larger neuromas occurred most frequently in the low tension groups (Fig. 2). The only normal-appearing nerves at reoperation were in the groups repaired with slight to moderate tension (tension 1, 2 and 3), and the most normal nerves appeared in the groups with tension of 2 and 3 (Fig. 3).

TABLE V. BRIEF SUMMARY OF ALL CASES WITH REOPERATION

NUMBER	NERVE	POSITION	TIME INJURY TO OPERATION (IN MO.)	TENSION	SUTURE MATERIAL AND TYPE	RESULT	REASON FOR REOPERATION	TIME AFTER FIRST OPERATION (IN MO.)	FINDINGS	OPERATION	RESULT
Cases With Tension of 4											
1	Radial	Mid-humerus	6	4+ Separ. 3 mm.	Silk stays, and epineural	Good	Condition of nerve at operation	6	Large neuroma	Lysis	Good
2	Peroneal	Popliteal space	16	4	Tantalum, epineural	No return	Suture line separation straightening knee	3	Separation 8 cm.	2-stage orrhaphy	No return
3	Sciatic	Mid-thigh	5	4	Silk, epineural	Poor	Poor return of function	17	Peroneal separated tibial small neuroma	Orrhaphy, peroneal	Inadequate f.u.
4	Ulnar	Mid-forearm	1 day	4+ Separ. 1 cm.	Silk, sling	Good	No return of sensation	4+	Nerve in continuity with irregular neuroma	Partial orrhaphy	Exellent
5	Tibial	Junction middle and lower 1/3 of calf	9+	4	Tantalum, sling and epineural	Fair	No return of sensation	10	Small, soft neuroma, continuity	Orrhaphy	Inadequate f.u.
Cases With Tension of 3											
6	Brachial plexus	Clavicle	5	3	Tantalum, sling and epineural	Poor	Poor return of function	15	Continuity scarring	Lysis	Inadequate f.u.
7	Peroneal, common	Head of fibula	7	3	Silk, epineural	Poor	Poor result	8½	Separation 7.5 cm.	Orrhaphy, 2-stage	Poor
8	Peroneal	Popliteal	11	3	Silk stay, epineural	No motor return	No motor return	8	Continuity	Orrhaphy	Inadequate f.u.

9	Median, radialus, ulnar, and cutaneous	Axilla	4	3	Silk stay, epineural	Insufficient time	2nd stage neurorrhaphy on ulnar nerve	1	Suture line could not be distinguished from normal nerve	Orrhaphy, ulnar	Advance Tinel's sign. Inadequate f.u.
10	Sciatic	Upper ⅓ of thigh	15	3	Silk stay, epineural	Sensation and advance of Tinel's sign	Condition at first operation	8	Nerve scarred greatly, length of suture line could not be distinguished	Lysis	Inadequate f.u.
11	Median and ulnar	Mid ⅓ of arm	3½	3 1	Tantalum, sling and tantalum foil	Fair Poor	Causalgia and trigger point	7	Small neuroma Large neuroma	Foil replaced, Foil removed	Reoperation after 9 mo. for trigger point, good result median, poor result ulnar
12	Sciatic	Mid ⅓ of thigh	4½	3	Silk, epineural	Good tibial, no return, peroneal	No return, peroneal	17	Large neuroma of tibial, separation peroneal 7 cm.	Lysis Orrhaphy	Good Poor
					Cases With Tension of 2						
13	Median and ulnar	Upper ⅓ of arm	12	2	Unknown	Good No return	Poor result, ulnar	15	Both intact Ulnar scarred	Lysis Orrhaphy	Inadequate f.u.
14	Radial	Lower ⅓ of arm	6	2	Unknown	Fair	No improvement after 6 mo.	15	Large neuroma	Lysis	Inadequate f.u.

(Table V continued on following page)

TABLE V—CONT'D

NUMBER	NERVE	POSITION	TIME INJURY TO OPERATION (IN MO.)	TENSION	SUTURE MATERIAL AND TYPE	RESULT	REASON FOR REOPERATION	TIME AFTER FIRST OPERATION (IN MO.)	FINDINGS	OPERATION	RESULT
15	Peroneal	Lower ⅓ of thigh	6	2	Silk, epineural	No return	No return	6	Large neuroma	Orrhaphy	Inadequate f.u. but beginning sensory return and Tinel's sign
16	Sciatic	Upper ⅓ of thigh	3½	2	Silk stay, epineural tantalum	Fair	Return not considered satisfactory	13	Small neuroma	Lysis	Good
17	Ulnar	Lower ⅓ of arm	3	2	Tantalum wire, tantalum foil cuff	Fair but trigger point	Trigger point	13	Suture line could not be identified	Removal foil	Good
18	Ulnar	Mid ⅓ of arm	6½	2	Unknown	No return	No return	11	Suture intact without neuroma	Lysis	Inadequate f.u.
19	Peroneal	Popliteal space	5	2	Unknown	Tinel's and sensory return	No motor function	16	Hard neuroma	Lysis	No further return
					Cases With Tension of 1						
20	Median		9	1	Tantalum wire, cotton epineural	Fair	No recent improvement		Partial separation	Partial orrhaphy	Exellent

21	Ulnar	Lower ⅓ of arm	1	1	Tantalum sling, epineural	No return	No return	5	Moderate neuroma	Orrhaphy	Good
22	Ulnar	Mid-fore-arm	7	1	Silk stays in sheath, epineural	No return	2nd stage on median nerve	2	Intact with small neuroma	None	Fair inadequate f.u.
					Cases With Tension of 0						
23	Median and Ulnar	Axilla	1	0	Tantalum wire, epineural, and foil cuff	No return	Neurorrhaphy Radial nerve	7	Intact without neuroma Narrowing due to foil	Removal foil	Inadequate f.u. but beginning return function
24	Ulnar	Wrist	2	0	Fine silk	Unknown	Neurolysis	3	Diffuse, hard neuroma	Neurolysis	Good
25	Ulnar	Lower ⅓ of arm	4	0	Silk stays in sheath, epineural	Poor	Slow return function	12	Small, soft neuroma	Lysis	Fair to good
26	Ulnar	Upper ⅓ of fore-arm	3½	0	Tantalum	Poor	Trigger point	13	Large, hard neuroma	Orrhaphy	Good
27	Peroneal	Popliteal space	6	0	Unknown	No return	No return	9	Partial, almost complete separation	Orrhaphy	Separation suture line 3rd neurorrhaphy without return function
28	Radial	Lower ⅓ of arm	3	0	Tantalum, and cotton	Fair	No improvement in 6 months	16	Scarring moderate	Lysis	No return

OTHER FACTORS CONSIDERED

It is well recognized that many other factors beside tension affect the end result in nerve repair. Most of these were considered in this study and were found to be essentially equalized in the various groups. Under similar conditions of repair, the radial, median, and sciatic nerves will give more satisfactory results than the ulnar, tibial, and peroneal nerves. It will be noted (Table VI) that the number of satisfactory and unsatisfactory result nerves are practically identical in each tension group.

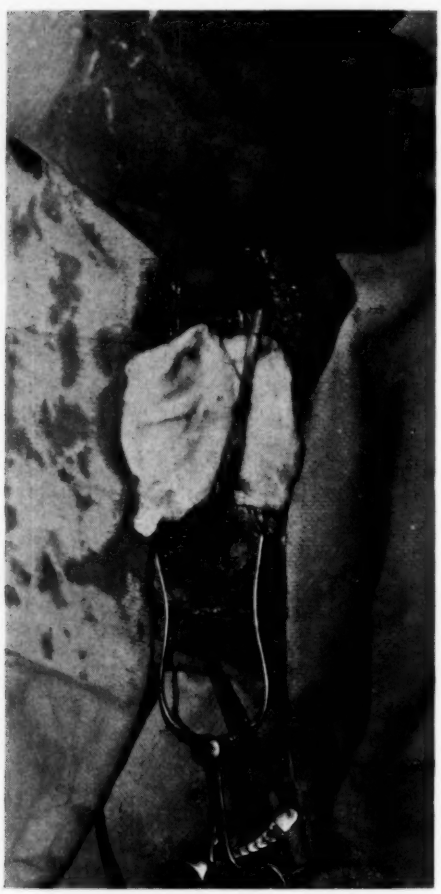

Fig. 2.

Fig. 3.

Fig. 2 (Case 22).—Ulnar nerve with small fusiform neuroma at suture site, two months after neurorrhaphy.

Fig. 3 (Case 9).—Median nerve at reoperation, three months after neurorrhaphy, with a tension of 3. Note the smooth contour without evidence of separation or neuroma formation.

The use of multiple stage procedures will be a factor in the result of nerve repair. As would be expected, two-stage procedures were used most frequently in the nerves with the largest gaps and so the greatest tension. Thus, in the groups with tension of 2, 3, and 4, the relative frequency of one-stage to two-stage procedures was respectively, 5:1, 3:1 and 8:1; while in the groups with tension of 0 and 1, the relative frequency in both was 18:1.

In reviewing the cases, it seems apparent that better results might have been expected if more two-stage procedures had been used in the maximum tension group.

Another factor which may affect the result is the suture material and the type of sutures used. Silk sutures were used most frequently in the cases in this series, especially those treated at Wakeman General Hospital. Sling sutures, through the nerve substance, were used rarely. The procedure of

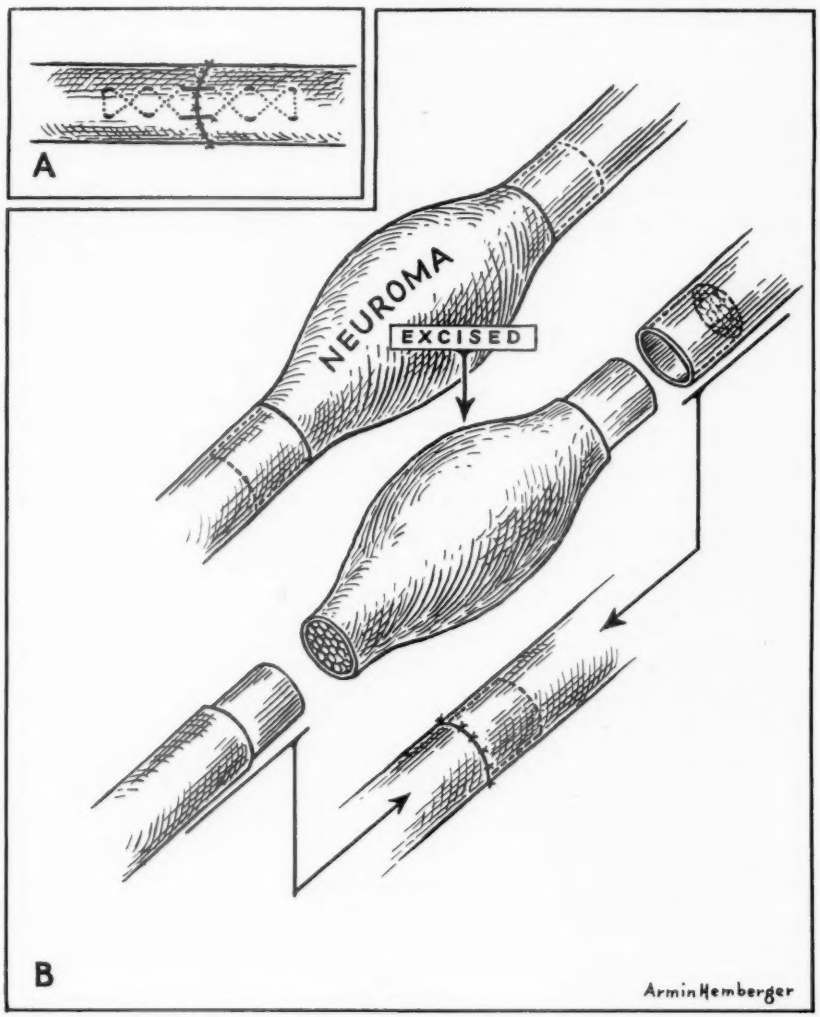

Fig. 4.—*A*, Drawing to illustrate the method used to place stay sutures in the nerve sheath, in cases with marked tension. *B*, Drawing to illustrate suture as performed with the dissected nerve sheath as a cuff.

choice in nerves under tension was considered to be the use of stay sutures of silk, usually 0 or 00 silk in the sheath. These stay sutures were placed as shown (Fig. 4, *A*) with the tension applied at some distance from the end of the nerve. With less tension, simple mattress sutures or interrupted sutures of 0 silk in the sheath, placed away from the nerve end, were used as stay sutures. The sheath was then approximated using 000000 silk either as inter-

TABLE VI. NUMBER OF POOR AND GOOD RESULT NERVES IN EACH TENSION GROUP

TENSION	SATISFACTORY NERVES (RADIAL, MEDIAN, SCIATIC)	UNSATISFACTORY NERVES (TIBIAL, PERONEAL, ULNAR)
0	26	33
1	25	25
2	47	46
3	35	36
4	9	12
Total cases	142	152

rupted sutures or as a continuous suture. These sutures were placed so as to evert the sheath and leave a smooth closure with the least possible gap for scar tissue to enter. An apparently more desirable procedure was carried out in a few cases. An elongated cuff was made from the sheath at one end, usually the proximal, while a similar length of nerve was denuded of sheath at the opposite end, and the sheaths were then sutured at a point distant from the point of contact of the nerve fibrils (Fig. 4, *B*). This method should leave the nerve fibrils at their point of contact ideally situated, according to the criteria of Weiss,[22] in a normal sheath with a slight gap filled with serum, separating their ends.

The condition of the nerve ends at the time of suture was considered of such importance that frozen section was done on as many cases as possible at Wakeman General Hospital. The number of cases in which the condition of the nerve is recorded is so small (102) as to be of doubtful significance. In almost all the cases studied, the nerve ends were fair or good, and the percentage of each type in the different groups was essentially the same except in the group with a tension of 3 (Table VII).

TABLE VII. CASES IN WHICH FROZEN SECTIONS WERE PERFORMED*

CONDITION OF NERVE		DEGREE OF TENSION									
		0		1		2		3		4	
		NO. OF CASES	PER CENT	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT	NO. OF CASES	PER CENT
Poor	A	0		2	11.7	1	3.6	8	24.2	0	
Fair	B	5	33.3	5	29.4	10	35.7	16	48.5	3	33.33
Good	C	10	66.6	10	58.8	17	60.7	9	27.3	6	66.66
Normal	D	0		0		0		0		0	

*Arranged according to the condition of the nerve and the tension used. The percentages are on the basis of the total number of cases in each tension group. The letters A, B, C, and D are used to indicate the condition of the nerve ends as follows:

A indicates unmyelinated, disoriented, scarred nerve fibers with much fibrosis, or scar tissue without nerve fibers;
B indicates some formed nerve trunks partially myelinated or unmyelinated with a moderate to marked fibrous tissue reaction around and among them;
C indicates many well-formed nerve trunks containing myelinated fibers with a small to moderate amount of surrounding fibrous tissue;
D indicates normal nerve.

The damage to other tissues including muscles, tendons, and bones, as well as vascular injury and joint involvement were evaluated and no significant difference was found in the five tension groups.

The vascular supply of the nerve may affect the result in neurorrhaphy. Although it has been shown that in ordinary nerve dissections the external

blood supply for a long section of nerve may be lost, without seriously affecting the result,[15, 16, 17] a similar loss may be an important factor in the results following repair of nerves under tension. This is not dissimilar to the results of nerve damage associated with the use of a tourniquet, where it was found that an injury which would not cause paralysis with normal circulation would cause paralysis if the blood supply were cut off by a tourniquet.[18, 19] A limited exposure of the nerve will prevent serious vascular damage in most instances. Dissection of the nerve for long distances probably enables one to place less tension on the suture line, but there will be more vascular damage and, in addition, the nerve will become fixed by scar tissue which will prevent stretching of the nerve and place increased tension on the short, uninvolved portion of nerve. With a limited exposure, a shorter section of nerve is fixed by scar, leaving a longer segment of relatively normal nerve to stretch in a smooth, undissected sheath.

Another factor which may affect the result in any neurorrhaphy is the relative position of the injury on the nerve trunk. Suture lines at or near the midpoint of the nerve are much more amenable to tension than those at either end, especially those near the proximal end. The tension will be the same on both sides of the suture line and this will cause greater relative stretch on the short than on the long limb. It is well recognized that the nerve roots will not stand as much tension as will the distal trunk. This fact is of great importance in high sciatic and brachial plexus injuries. Inequalities in length at the distal end may well explain the poor results in peroneal neurorrhaphies, as there is a very short trunk with sharp angulation between the branching of the sciatic and the multiple terminal motor branches of the peroneal.

The length of time of fixation and the method of straightening flexed joints has varied markedly from one group of nerve surgeons to another. It has been considered and proved experimentally that the suture line is as strong after two to three weeks as it will become.[20] Whether the joint is to be extended gradually by a controlled method such as a turnbuckle cast, or by the patient himself, has been the main subject of dispute. In the majority of the cases in this series, the extremities were kept in the position of choice by casts or splints for two to three weeks, depending upon the tension on the nerve, and then they were gradually extended by regulated exercises over a period of two to four weeks.

DISCUSSION

Although it has been considered that tension should not be placed on the suture line, there are some theoretical and experimental factors in favor of placing at least minimal tension on the suture line. If the nerve is completely lax, the nerve fibrils may buckle, causing them to grow laterally or in a direction other than downward into the distal trunk.[21] Weiss,[22] in his discussion of the plasma clot method of suture, mentioned as one of the advantages of this method the tendency of the nerve to retract, putting the fibrin strands of the plasma clot on a stretch and giving the nerve fibrils a straight path

into the distal stump. The same should hold true with a suture line under tension, the epineurium being in close approximation with the nerve fibrils tending to pull apart in a serum blood clot.

It has been suggested that even if the suture line holds, the tension on the nerve itself will result in irreparable damage, because of tearing of nerve fibrils and hemorrhage.[1, 2, 3] By experiment, this has been more or less disproved. Denny[23] showed on the intact nerve that hemorrhage occurred rarely, only with extreme tension, and that the first structure to give way was the sheath rather than the nerve fibrils themselves. With marked tension there was beading of the nerve fibrils, but no actual tear. Even with a stretch sufficient to increase the nerve length 100 per cent there was paralysis beginning twenty-four hours after the injury but complete return of function within two months. Takimoto[24] showed that a tension equivalent to a weight of 32 kg. was necessary to cause a temporary loss of function. Mitchell[25] stated that a nerve could be stretched three-quarters inch for each two inches of length. Sanders[6] and Frazier[5] came to the conclusion (from clinical material) that moderate stretch of the nerve was not too detrimental. Sanders suggested a stretch of 10 per cent of the mobilized length of the nerve might be applied without damage but that 30 per cent might be harmful even if applied in two stages. Frazier stated the maximum stretch should not exceed 7 to 8 cm. Although many of the cases of this series, especially those in the group with a tension of 4, exceeded the 10 per cent or 7 to 8 cm. maxima, they never approached the tension indicated by the other authors. The following case is of interest in this regard.

CASE 29.—This soldier had a severe guttering wound of the medial side of the ankle and foot. At exploration, the nerve ends were found to be separated by 14 cm. and after excision of neuromas, the gap was 16 cm. After mobilization of the nerve to the popliteal space, it was possible to suture the tibial trunk to the plantar nerves with a tension of 3; 0 silk stay sutures and a 000000 silk running lock stitch in the sheath were used. Unfortunately, the patient developed miningitis and succumbed on the fourth postoperative day. At post mortem, the suture lines were intact and sealed off by fibrin without evidence of separation or pulling of the sutures. The nerve appeared normal throughout its length and sections taken from several points along its length revealed normal nerve structure.

This case, with its complete pathologic study, tends to support the opinion of those who hold that definite tension need not seriously damage a nerve. The end results in this series of cases indicate that this opinion is valid and that, if necessary, one should not hesitate to apply tension in order to approximate the ends of the nerve in neurorrhaphy.

CONCLUSIONS

1. Slight to moderate tension on the suture line in peripheral nerve surgery is not harmful and may be beneficial, with proper attention to detail in the repair.

2. Maximum tension, although not desirable, may result in satisfactory return of function, even in the occasional case with a small gap remaining between the nerve ends.

3. Maximum tension on the suture line is probably preferable to a nerve graft in the human being.

4. A method of suture for use in neurorrhaphy is described. No cases in which this method was used had suture line separation even with maximal tension.

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SOME DISABILITIES OF THE KNEE

A Statistical Survey

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DISABILITY of the knee joint, as the result of disease or injury, is not an uncommon problem presented to the general surgeon. Therefore it is desired to present some clinical data of patients with internal derangement of the knee joint, and to indicate the uses of a simply constructed dynamometer as it may be applied in the treatment of such disabilities.

There were 283 patients, or 1.5 per cent of 5,467 patients, admitted to Oliver General Hospital, Augusta, Ga., during a period of eleven months in 1943, with disability of the knee joint. These were divided as follows: arthritis 42, synovitis 57, sprain and strain 13, dislocation of patella 2, interstitial calcification about the knee joint 6, psychosomatic disease[1] 17, and internal derangement of the knee joint 146. Of the latter, 73 patients not selected for operation were treated conservatively by bed rest, traction, cast, aspiration, graduated physiotherapy, and muscle training. In the course of rehabilitation an estimation of the rate of recovery of the quadriceps muscle group, and later the weight-bearing power of the extremity, can be aided by objective muscle power tests.

Evaluation of the Extensor Mechanism of the Knee, a Muscle Power Test

Correction of pathologic conditions responsible for internal derangement without undue delay is important, but equally necessary before secure unlimited function can be obtained is recovery of lost muscle power and volume which invariably affects the extensor mechanism of an injured knee.[2, 13] The difficulty in estimating the extent and rate of recovery prompted the improvision of a circular scale with a short acting gravity lever (approximately 14 inches) as a dynamometer (Fig. 1) for measuring the power of the quadriceps and associated groups of muscles. In performing the spring scale test the warmth of the leg was determined by palpation, and previous measurements of the circumference of the thigh and leg were checked. The tests were not made in the presence of other patients, the patient was unable to observe the recording of the scale, and no comments were made except encouragement to produce maximum muscular contraction.

The results of innumerable tests on forty patients during their reconditioning process indicated certain permissible inferences: (1) The maximum extensor strength of the thigh muscles ranges from 50 to 150 pounds. (2) The progress of muscle restoration can be accurately charted by repeated examinations. (3) The response to massage, physical therapy, and exercise may be observed by detecting differences of muscle strength at interval re-examinations. (4) Excessive treatment or exercise may be first noticed by failure of increasing muscular power. During periods of inactivity little change, and sometimes

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rapid diminution in muscle power, was recorded. Failure to work, or the employment of protection of the extremity by the patient, is reflected by no increase in power. (5) The height and weight of the patient are not significant in determining the power of the quadriceps. (6) Atrophy does not indicate the actual power of the quadriceps extensor group. Increment in muscle strength has followed industrious quadriceps exercise with 25 to 50 per cent increase in muscle power without increase in the volume of the thigh muscles.

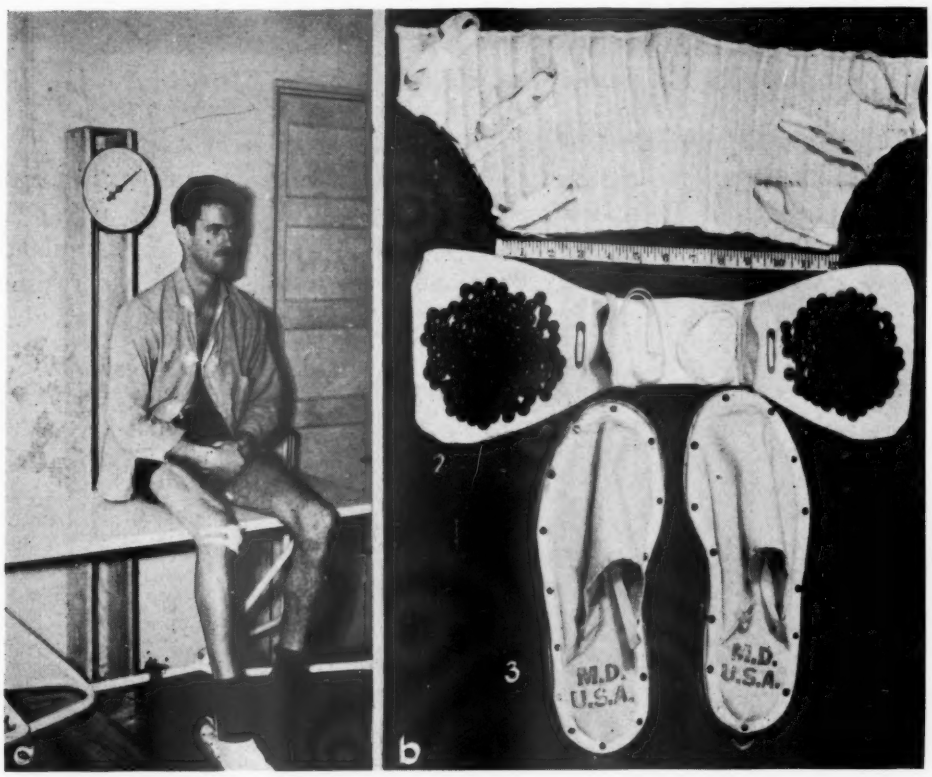

Fig. 1.—*a*, Inexpensive spring scale used as dynamometer for testing quadriceps muscle. *b*:*1*, Short canvas legging fluted to carry lead shot; *2*, canvas bag for lead shot of variable weight as desired; *3*, Hospital slipper nailed to wooden sole for use in spring scale test.

Subsequently it was learned that an adaptation of the spring scale test described by Lovett[14, 15] had been improvised. Recently Schmier[16] and Milch[17] have employed more efficiently the same principle for assessing muscular strength. Lewey[18] has determined the reliability of the spring scale method by means of a comparative study with the use of the electromyogram. He plotted the value of the two methods against each other and showed the close relationship between electromotive force and voluntary muscular contraction.

SELECTION AND PREPARATION OF PATIENTS FOR MENISCECTOMY

In general it may be stated that a careful estimate of the patient in the light of his occupation, his attitude, desire for work, physical and technical fitness have a direct bearing upon the usefulness of an operation. Largely

patients were selected for meniscectomy whose injury had been incurred in line of duty, and were not complicated by associated injuries such as osteochondritis dissecans, instability of the knee joint as the result of injury to the cruciate or collateral ligaments, arthritis, chondromalacia of the patella, or severe traumatic synovitis.[19] In addition to the usual preoperative care, attention was given to the correction of hypotonia and atrophy of the quadriceps extensor muscles, in an effort to achieve some preoperative restoration of muscle function and to have the patient well trained for postoperative exercises. Each case was individualized and desirable nonweight-bearing exercises were instituted.

Exercises.—

1. Quadriceps extensor setting, 1,000 or more times a day.
2. Patient supine in bed, flexes the thigh to right angle and with weighted bag tied to the foot he slowly extends and flexes the leg.
3. Patient prone in bed, foot in slipper which is attached through a pulley to a weighted bag, actively flexes and extends the leg against resistance (Fig. 2).

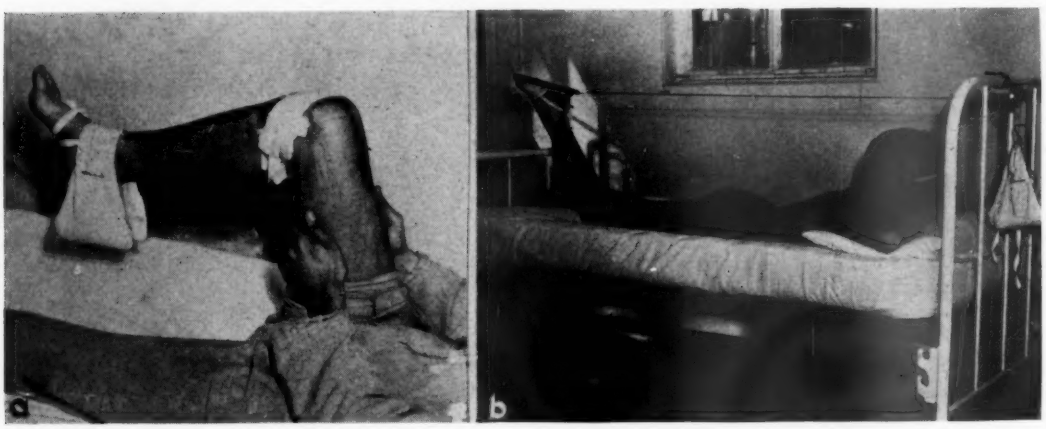

Fig. 2.—*a*, Nonweight-bearing exercises using weighted bag. *b*, Weighted bag and pully with slipper for leg and thigh exercises.

Such nonweight-bearing exercises when employed strenuously were not associated with signs of joint irritation or subjective complaints. Progress was checked by measurements of the leg volume and the dynamometer tests.

MENISCECTOMY

Two instruments were constructed (Fig. 3) from sharp periosteal elevators for excision of the medial semilunar cartilage through an anterior incision into the joint. A modified Jones incision was used in the skin. The incision into the joint extended from a point, the leg hanging at a right angle, 1.5 cm. medial to the apical attachment of the ligamentum patellae obliquely downward and posterior, dividing the fibrous fanlike membrane of the tibial collateral ligament[20] and ending at the parallel fibers on a level with the

coronary ligament. The cartilage was usually freed anteriorly with ease. The liberation of the central portion of the cartilage was begun by the delineation of the superior and inferior capsular reflections which were separately divided along the periphery of the cartilage by the broad sharp dissector. By means of traction tension on the cartilage the areolar tissue binding the cartilage to the parallel portion of the tibial collateral ligament is made taut and easily separated with the dissector.

The oblique portion of the tibial collateral ligament is inseparably united to the joint capsule posteriorly and, accordingly, has been demonstrated[21, 22] to be joined to the meniscus. The knee is hyperflexed, allowing the tibial collateral ligament to slide backward permitting easier access to the posterior

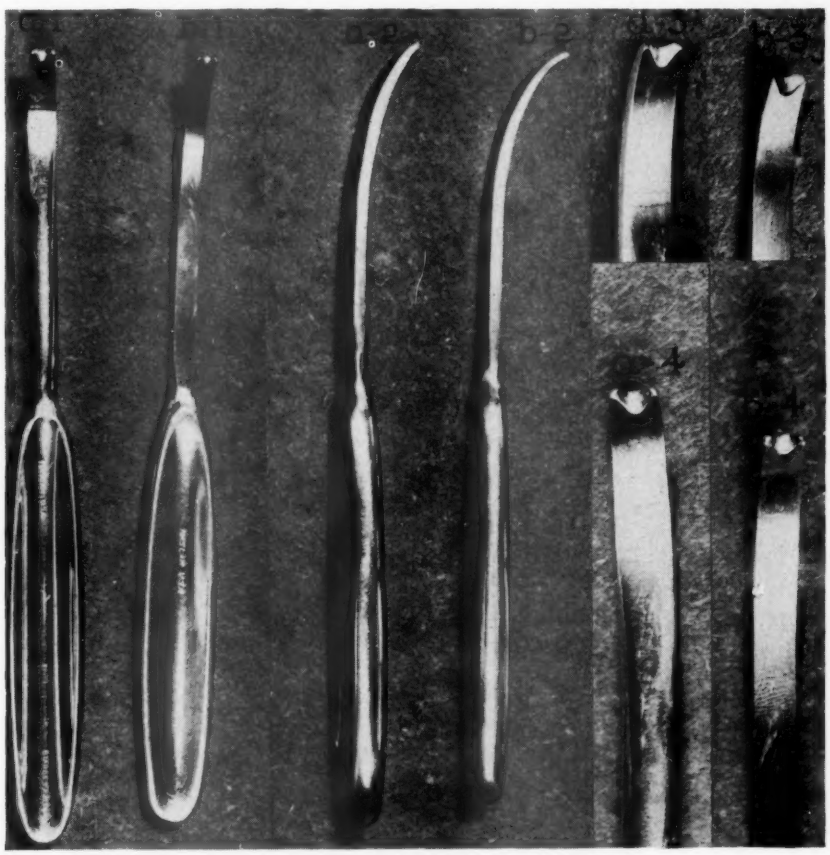

Fig. 3.—Photograph of cartilage dissectors. *a-1*, 4/5 actual size, broad dissector; *b-1*, 4/5 actual size, narrow dissector; *a-2*, side view, curved approximately 115 degrees; *b-2*, curved approximately 130 degrees; *a-3*, enlarged 1 2/5 times; *b-3*, oblique view of concave cutting edge showing blunted outer margins; *a-4*, and *b-4*, end view, enlarged 1 2/5 times.

capsular attachment of the cartilage. The limited exposure could be further improved by adduction or abduction and rotation of the tibia on the femur, combined with digital pressure on the posterior joint capsule. The narrow dissector was employed to divide the superior and inferior capsular folds and the fibrous tissue uniting the capsule and the fibrocartilage. The freed cartilage is dislocated into the intercondylar notch, and its posterior limb between the

lateral meniscus and the posterior curciate ligament is divided under direct vision with the broad dissector. These instruments were a satisfactory addition to the usual devices employed to remove the semilunar cartilage.*

Forty-one of forty-nine patients operated upon for internal derangement of the knee joint were found to have injuries of the semilunar cartilage. The meniscus injuries were divided into three groups; longitudinal tears, completely avulsed except for anterior and posterior attachments, and loose semilunar cartilages.

The largest group, thirteen of forty-one patients, sustained longitudinal tears of the semilunar cartilage of the bucket handle type. The average duration of disease was fourteen months. The symptoms and clinical findings were fairly constant and permitted an accurate diagnosis.

Completely avulsed cartilages attached anteriorly and posteriorly with the free portion lying in the intracondylar notch were found in eight cases. There were five patients with tears of the anterior portion of the cartilage, six with tears of the middle portion, and four posterior cartilage tears. These men had sustained their injuries twenty-one months prior to an average of fifty-two hospital days before surgery. In this analysis there were no characteristic complaints or findings on physical examination which would permit a diagnosis of the position of a partial tear of the cartilage. Brown[25] has reported the unreliability of McMurray's sign in tears of the posterior portion of the cartilage. In the absence of finding an accountable lesion in the anterior joint compartment the surgeon is committed to removal of the entire cartilage on the suspicion of a posterior tear.

In five cases examination of the menisci at operation showed no fracture or dislocation of the cartilage but there was definite looseness beyond that considered normal. In addition the infrapatellar fat pad and adjacent synovium were hypertrophied; the cause of disability was undetermined. The history of these patients was not unlike that given for longitudinal tears of the cartilage. Two patients were found to have hypertrophy of the infrapatellar fat pad in the absence of any injury to the cruciate ligaments or abnormality of the semilunar cartilages. The history and physical examination were not pathognomonic of the condition found at operation. A recurrent cyst of the lateral cartilage which proved to have been incompletely removed and connected with the lateral cartilage was totally removed by means of two incisions into the joint capsule as employed by Cave and others.[26, 29]

SUMMARY OF FOLLOW-UP STUDY

A follow-up questionnaire, prompted by an earlier experience,[30] was sent through military channels to each man three months or more after leaving the hospital. Sixty-five per cent replied. A subsequent study by Cave and others shows the thoroughness of such follow-up studies when pursued with uninterrupted continuity of effort. At the time this study was terminated† 105

*Morrison[23] and Dowing[24] have recently described semilunar cartilage knives. Downing's knife has two blunt guides so that one passes under the meniscus and the other over the meniscus and internal to the synovial fold, thus with the knee acutely flexed the curved blade frees the meniscus from its posterior peripheral attachment and there remains only its central posterior attachment to be divided.

†An overseas assignment precluded the termination of this work as planned.

men were returned to duty and 94 were separated from the service for disability; of these, 112 to whom questionnaires were sent had been discharged from the hospital four or more months. Seventy-one replies were received. These indicate 60 per cent had continued military duty. Less than 60 per cent of the men separated from the service returned their questionnaires; however, 90 per cent of those who replied were performing work comparable to limited military service.

SUMMARY

More than 50 per cent of knee disabilities, excluding fracture and dislocation, were found to be the result of internal derangement; of these one-half required surgical treatment.

Meniscectomy is an essential part of correcting internal derangement of the knee joint but in the absence of restoration of quadriceps muscle strength, full weight-bearing power of the leg will be delayed. Surgeons are generally careless as applied physiologists in combining surgical intervention and accepted means of restoring quadriceps muscle power in the treatment of knee joint disability. Postmeniscectomy complaints in eighteen men were found to be due in more than one-half to quadriceps atrophy and in two because of incomplete removal of the semilunar cartilage.

The spring scale muscle test is suitable for employment as an objective means of determining the progress of quadriceps muscle recovery after injury or arthrotomy of the knee joint. Failure to assay correctly quadriceps restoration may be the result of not employing such subjective measurements.

Undue delay of chondrectomy is undesirable as it allows development of quadriceps atrophy and often trauma to the articular surfaces of the femur.

An adequate follow-up study on all patients treated in military hospitals and also those separated from the service is desirable in order to conserve the fighting strength of the army by ascertaining the effect of improved surgical and medical treatment.

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OLD UNITED AND UNUNITED FRACTURES OF THE PATELLA

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THERE are very few references in the literature about the treatment of ununited fractures of the patella before the development of aseptic surgery.[1] Nonunions after patellar fractures were so common that they were accepted as good results. In 1878, Wyeth[2] reported an unsuccessful attempt to obtain bony union by injection of sheep marrow between the fragments. In 1881, 2 cases of ununited fracture of the patella were reported[3] in which fixation of the fragments with silver wire was successful. Internal fixation gradually became accepted as the treatment of choice and the only disagreement among surgeons concerned the method to be used. Various surgeons reported their techniques and each one felt that his method was the best.[4-6] In 1915, Phemister[7] reported on the use of grafts of free fascia lata to connect the fragments. In 1927, Gallie and LeMesurier[8] reported their method of repair; they used fascia or a segment of the Achilles tendon. In 1928, Albee[9] recommended the use of an autogenous bone graft to hold the fragments and stimulate union.

The value of partial excision of the patella in treating ununited fractures was recognized shortly after Thomson[10] reported its use for acute fractures in 1935. Since then, Miltner[11] and Prince[12] have recommended partial excision for ununited fractures. Total excision of the patella for ununited fractures was reported as early as 1908 by Rogers.[13] He made two very bold statements for his time: (1) "The patella can be removed when ununited and perfect flexion and extension procured," and, (2) "The patella should be removed when ununited or when repeated fracturing occurs." This method of treating ununited fractures did not gain favor until, as a result of Brooke's articles in 1937,[14, 15] total excision became more widely used for acute fractures. In 1938, Tippett[16] reported 3 cases in which ununited fractures were treated by total excision. In 1941, the same surgeon[17] recommended total excision of the patella in a case of fracture of the patella complicated by patellofemoral arthritis. In 1942, Wass and Davies[18] preferred total excision as the treatment for, "selected cases of patellofemoral arthritis following malunited fractures." In 1946, Horwitz and Lambert[19] and MacAusland[20] reported good results in cases of ununited and old fractures of the patella treated by total excision.

CLINICAL FINDINGS

Forty-two patients came to the Mayo Clinic between January, 1910, and January, 1946, because of old fractures of the patella. Thirty-eight of these patients had old ununited fractures and 4 had old united fractures. The majority of the patients had symptoms and signs of osteo-arthritis in the involved patellofemoral joint. The static pain, limited motion, and muscular

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atrophy from which these patients suffered were typical of this type of arthritis. However, roentgenograms in most instances did not show evidence of marked osteo-arthritic changes. In the 4 cases of old united fractures, there were varying degrees of irregularity and hypertrophic changes in the patello-femoral joint. Longitudinal or chip fractures did not occur in this series, which suggests that in fractures of this type the fragments almost always unite, or at least when they do not unite disability does not result.

It was possible to treat 11 patients by conservative measures. In each case, the fracture did not involve the articular surface and the symptoms and signs were minimal. Some form of operation was advised for the remaining 31 patients. Eight patients with ununited fractures and 1 patient with patello-femoral arthritis, the result of an old united fracture, were advised to have surgical treatment but refused. Eight patients with old ununited fractures were treated by internal fixation using beef bone screws, catgut, silk, or silver wire. Nine patients were treated by excision of the smaller fragment or fragments. Five patellectomies were done: 2 in cases of ununited fractures and 3 in cases of old united fractures with patellofemoral arthritis.

Thirty-one of the 42 patients were traced for an average of 9.1 years. The results are shown in Table I. All of the patients treated by conservative measures obtained good results. Three of the 9 patients who refused to have surgical treatment were traced for an average of 9.0 years. In each case the condition was much worse, and the symptoms were those of osteo-arthritis. Seven of 8 patients treated by internal fixation were traced for an average of 12.3 years. In 4 cases the condition was not improved and in 2 there was some improvement; the result was excellent in only 1 case. Seven of the 9 patients treated by partial excision were traced for an average of 6.5 years. In 2 cases the results were excellent, in 4 cases the patients improved, and 1 patient was no better after operation than before. The 5 patients who underwent patellectomy were traced for an average of only 1.6 years. In this short period, 3 were improved and in the other 2 cases the 2 results were considered excellent. On the basis of the relatively few patients, we see that partial excision of ununited fractures resulted in more improved patients than did the attempts at internal fixation. Total excision gave good results in both ununited fractures and symptomatic old united fractures.

TABLE I. RESULTS OF THE TREATMENT OF PATIENTS WITH OLD FRACTURES OF THE PATELLA

METHOD	PATIENTS	TRACED PATIENTS	AVERAGE FOLLOW-UP (YR.)	RESULTS		
				EXCELLENT	IMPROVED	NOT IMPROVED
Reassurance and physical therapy	11	9	12.7	4	5	
Surgery advised but patient refused	9	3	9.0			3
Internal fixation of fragments	8	7	12.3	1	2	4
Excision of smaller fragment or fragments	9	7	6.5	2	4	1
Total excision of patella	5	5	1.6	2	3	
Total	42	31	9.1	9	14	8

PATHOLOGIC ASPECTS

Specimens from 15 patients were available for gross and microscopic study. In 9 cases the patients had undergone partial excision for nonunion. In 5 cases the entire patellas were studied; in 2 there was nonunion and in 3 there was union with patellofemoral arthritis. Replacement of articular cartilage by fibrous tissue was the predominating finding on gross examination. The remaining cartilage showed evidence of degeneration such as furrowing and fraying. In some specimens erosion extended through to subchondral bone. The varying degrees of distortion of the normal gross outline and contour of the specimens probably contributed to the development of arthritis by upsetting the normal mechanics of the patellofemoral joint. Mild hypertrophic lipping of the borders of the articular surface was present in only 1 specimen.

Microscopically, in 13 of 15 specimens, degeneration of the cartilage had taken place which was considered more marked than normal for the age of the patient. The work by Bennett and associates[21] on changes in the knee joint at various ages was used as a basis for the comparison. Whether or not we should label the changes in the patella "osteo-arthritis" (degenerative arthritis) or "traumatic arthritis" is an interesting problem. The altered staining, clumping of cells, fissuring and fraying, irregularity of the bone-cartilage zone, and the replacement of degenerating cartilage by fibrous tissue are similar to the findings of Bennett and associates[21] and Allison and one of us (R. K. G.)[22] in degenerative (osteo-) arthritis. However, in the articular cartilage of the patellas in our series, the fibrous-tissue replacement seemed to be the predominant finding. In some specimens fibrous tissue covered the surface of the hyaline cartilage and in some areas it filled in large defects in the cartilage. Moreover, the changes seemed to be imperfect attempts at repair rather than pure degeneration. There were many evidences of repair after trauma to the patellas. The displacement of cartilage into cancellous bone and replacement of the cartilage by bone is a very good example. The clefts filled with fibrous tissue are also examples. In his study of "amputated specimens obtained after severe injury," Soto-Hall[23] observed "linear fractures" of articular cartilage and believed they might be factors in producing degeneration. Cox[24] suggested that trauma to the patella might cause fractures in the "minute girders" of cancellous subchondral bone and result in impairment of nutrition and degeneration.

There is experimental evidence to indicate that arthritis will develop after single traumatic insults. Key[25] produced what he called "hypertrophic arthritis" in the patellofemoral joints of rabbits by creating defects in the patellar surface of the femur. Bennett and Bauer[4, 26] performed similar experiments in dogs and found that arthritis developed only when the patella was displaced from its bed. They said that cartilage cells have only "feeble ability" to proliferate. Experimentally created defects were healed by fibrous tissue which originated in "the connective tissue of the bone marrow, in the marginal synovial membrane, and apparently, in some instances, from articular cartilage cells."

In the present study it was difficult to be certain where the fibrous tissue originated. The clefts and defects seemed to be filled with fibrous tissue arising from the marrow; at least, the fibrous tissue in the defects was continuous with the marrow. The surface fibrosis was connected with the surrounding synovia and with the fibrous tissue in the defects in the cartilage. Some fibrous tissue may have arisen from the site of the fracture during the process of healing. The fibrous tissue did not seem to arise from cartilage cells. It is impossible to say when the fibrous tissue was formed, but it was present in 1 patella examined four months after the initial injury.

Fig. 1 (Case 1).—*a*, An old fracture through the upper pole of the left patella with slight separation and tilting of the fragments. There is evidence of early union. *b*, The same knee two years later, showing consolidation of the fragments. Note the irregular articular surface of the patella.

REPORT OF CASES

CASE 1.—A physician, 29 years of age, came to the clinic in May, 1945. His chief complaint was stiffness in the left knee. The stiffness had resulted from twelve months' immobilization required to obtain union after a compound fracture of the left femur. The knee had been manipulated under anesthesia two months before the patient came to the clinic. He had experienced pain for two weeks after the manipulation and had noticed rather marked effusion.

On examination moderate atrophy of the left quadriceps was noted. The knee could be fully extended but could be flexed only 40 degrees. Roentgenograms of the left knee revealed evidence of an old fracture through the upper pole of the left patella with early union (Fig. 1, *a*).

The patient continued his duties as house surgeon during the next two years and was re-examined in May, 1947. There had been moderate pain in the knee for about two months. The pain was aggravated by walking, climbing stairs, and changes of weather. Results of

examination were essentially the same as before, there being only 40 degrees flexion. Roentgenograms revealed evidence of bony union at the site of the patellar fracture (Fig. 1, *b*), but the articular surface of the patella had become quite irregular. Accordingly, arthrotomy was performed through a median parapatellar incision. The articular surface of the patella was found to be soft and shaggy. There was almost complete loss of about 1.0 cm. of cartilage from the medial part and near the lower pole of the patella. The cartilage on the medial femoral condyle adjacent to the patellar erosion was eroded. The patella was excised and the median parapatellar incision in the capsule was closed without suturing the quadriceps tendon to the patellar tendon. Quadriceps-setting exercises were started on the second postoperative day. The patient played eighteen holes of golf four weeks after the operation. One year after patellectomy the patient had no pain except for that caused by changes of weather and that which occasionally followed climbing stairs. Full active extension and 100 degrees of flexion were present. Roentgenograms revealed no evidence of calcific or osseous foci in the quadriceps tendon (Fig. 2, *a*).

Fig. 2 (Case 1).—*a*, Same knee as in Fig. 1, twelve months after patellectomy. There are no calcific or osseous foci in the quadriceps tendon. *b*, Articular surface of the patella excised twenty-six months after a transverse fracture. Note the shaggy strands of tissue attached to the rough cartilage. The normal contour of the ridge and facets has been distorted.

Pathologic Aspects.—The general contour of the patella was slightly distorted and the articular cartilage was soft, rough, and irregular. Shaggy strands of tissue were attached to the surface, particularly in the proximal half (Fig. 2, *b*). Serial microscopic sections revealed a thin layer of vascular fibrous tissue that covered the hyaline cartilage in most areas. There was some fibrocartilage associated with the hyaline cartilage and there was moderate fibrillation of the matrix. The bone-cartilage zone was quite irregular and new lamellae of bone were being formed about small blood vessels in the zone of calcified cartilage (Fig. 3, *a*). The site of the fracture could be identified by a layer of hyaline cartilage that was displaced into the cancellous bone. This cartilage had been invaded by blood vessels and it was being replaced by bone (Fig. 3, *b*).

Comment.—This case serves as a good example of patellar fracture due to manipulation. The fracture was not discovered until malunion had occurred.

Two years later disabling patellofemoral arthritis was present. Patellectomy resulted in almost complete relief of pain and 60 degrees increase in motion.

The pathologic findings were those of traumatic arthritis.

CASE 2.—A professional football player, 25 years of age, first came to the clinic on May 27, 1932. He stated that three years and four months previously he had been thrown from his motorcycle and as he fell he struck the left knee against the concrete road. At the time he suffered moderate pain, but was able to walk and ride the motorcycle again. There was considerable soreness and tenderness in the patellar region for six months after the accident, but the patient did not consult a physician. On admission to the clinic, his

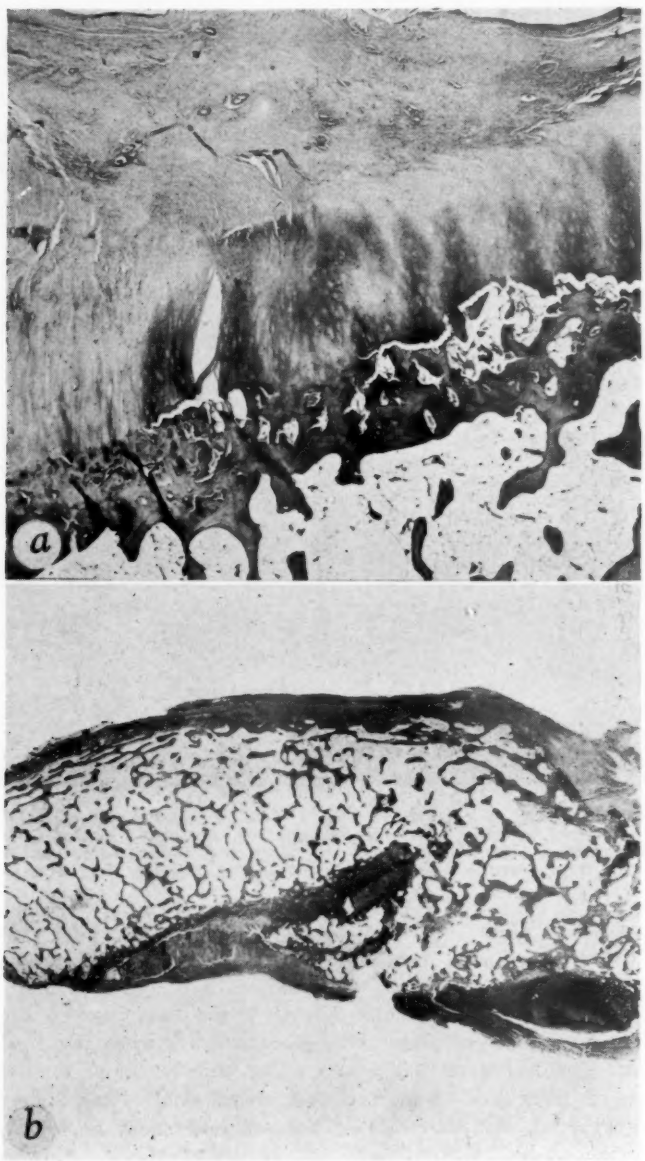

Fig. 3(Case 1).—*a*, A longitudinal section through the middle part of the medial facet which shows vascular fibrous tissue covering the surface of the hyaline cartilage. There are some irregular staining and fibrillation of the matrix. There is irregularity of the bone-cartilage zone (×16). *b*, A longitudinal section through the entire patella in the medial facet shows fibrous tissue covering and replacing articular cartilage. Note the articular cartilage displaced into the cancellous bone of the body of the patella (×25).

chief complaints were weakness when crouching and springing forward, and pain after prolonged exercise.

On examination he was found to have slight atrophy of the quadriceps. The upper border of the left patella was slightly tender and there was a palpable deformity in this region. There was a full range of active motion. Roentgenograms revealed an old ununited fracture of the proximal pole of the patella (Fig. 4).

Fig. 4.

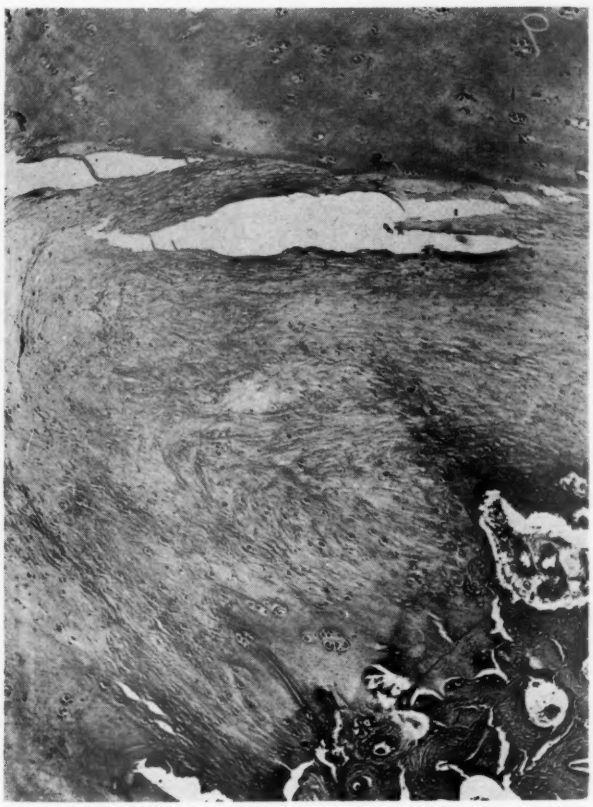

Fig. 5.

Fig. 4 (Case 2).—The left knee shows evidence of an old ununited fracture of the proximal pole of the patella with some separation and tilting of the fragments. Note the difference in density of the two fragments and the sclerosis along the fractured surface of the distal fragment.

Fig. 5 (Case 2).—A section through the center of the medial facet of the excised fragment, showing a wedge-shaped defect in the hyaline cartilage which has been filled in by fibrocartilage and fibrous tissue. Note the irregular bone-cartilage zone (×45).

Arthrotomy was performed and the proximal fourth of the patella was found "lying as a loose body in the quadriceps expansion." This fragment was excised and the tendinous structures were sutured back over the area. Active motion was started five weeks postoperatively, and the patient returned to professional football four months after surgery. In answer to a letter of inquiry fifteen years later the patient said he had slight pain on severe exertion but motion and strength were unlimited.

Pathologic Aspects.—Grossly, the articular surface of the excised fragment was uneven and furrowed. The surface of the fracture was covered with smooth fibrous tissue. Microscopically the articular cartilage was fissured and frayed and there was clumping of the cells. Fibrous tissue covered the surface in some areas and there were clefts and defects in the hyaline cartilage which were filled with fibrous tissue and fibrocartilage. The bone-cartilage zone was quite irregular (Fig. 5). A layer of avascular fibrous tissue covered the fracture surface. There was some fibrocartilage mixed with the fibrous tissue and the surface cells were arranged in a compact layer three to four cells deep, similar to synovial

tissue. It was interesting to find that the cancellous bone and marrow were normal in all respects, because, as was said, the fragment was found "lying as a loose body in the quadriceps expansion."

Comment.—The fracture was produced by a direct blow and there was no rent in the quadriceps expansion, which allowed rather good function with little disability. Excising the proximal fragment increased the strength of the knee and decreased the likelihood of disabling traumatic arthritis in subsequent years. Pathologically, there was evidence of early traumatic arthritis in the cartilage of the excised fragment.

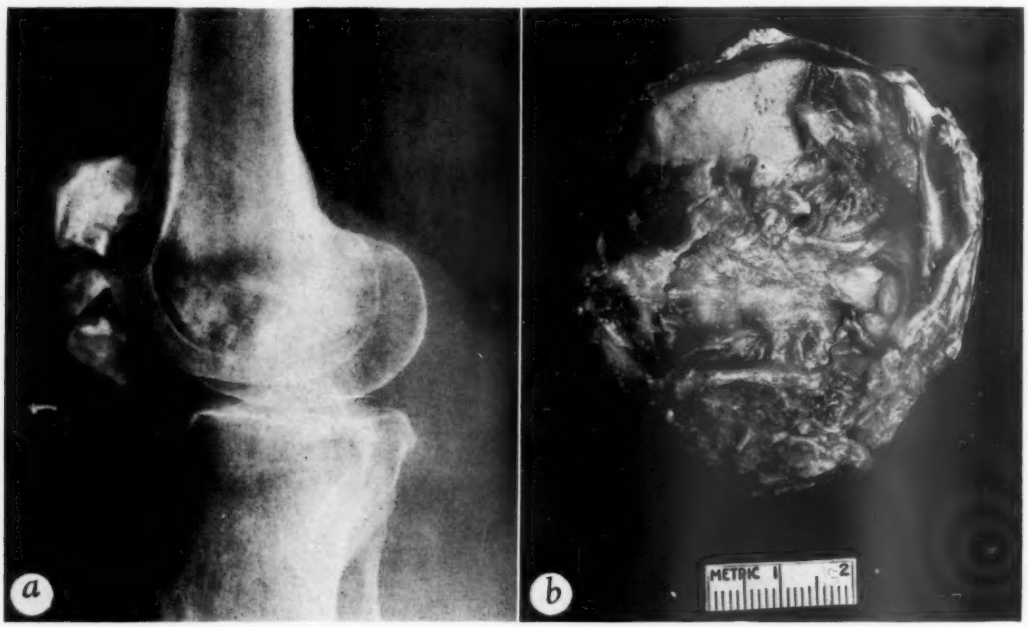

Fig. 6 (Case 3).—*a*, A ten-month-old comminuted fracture of the patella of the right knee with wide separation of the fragments. There is relative increased density of the proximal fragments and osteoporosis of the bones forming the knee joint. *b*, The entire articular surface of the right patella is covered with rough fibrous tissue except for a small area in the proximal portion of the medial facet, which is covered with rough pitted hyaline cartilage.

CASE 3.—A businessman, 49 years of age, came to the clinic on Feb. 7, 1946. His complaints were stiffness and pain in the right knee. Six months previous to his admission he had been in a head-on collision, and had suffered fractures of both bones of the left forearm, a compound fracture of the right femur, and a fracture of the right kneecap. The fractures of the forearm were treated by open reduction and internal fixation. The fractured femur was treated by traction for six weeks, after which a long leg spica cast was used for two and one-half months. The only treatment for the fractured patella had been the immobilization used to obtain union of the fractured femur.

The patient walked with a cane and had a limp caused by the injured right knee. On examination there was marked atrophy of the quadriceps muscle of the right thigh. The patient could extend the leg fully but flexion was limited to 10 degrees. The patella was moderately enlarged and irregular in outline. Roentgenograms revealed evidence of an old comminuted fracture of the right patella with separation of the fragments (Fig. 6, *a*).

Arthrotomy was performed through a median parapatellar incision and the entire patella was excised. After this the knee could be passively flexed 30 degrees. The wound was closed without joining the patellar and quadriceps tendon. Active and passive motion was started on the eleventh postoperative day and continued daily for six weeks, at the end of which time there was 30 degrees' active motion in the knee (180 to 150 degrees).

Six months later a letter from the referring physician revealed that motion remained the same. The patient did not return the questionnaire.

Pathologic Aspects.—Examination of the patella revealed gross deformity of the articular surface (Fig. 6, *b*). Microscopically, the articular surface was covered with fibrous tissue and some fibrocartilage. The hyaline cartilage which remained was covered with vascular fibrous tissue and contained clefts and defects filled with fibrous tissue. Union of the two major fragments was formed by fibrous tissue (Fig. 7).

Fig. 7 (Case 3).—A median longitudinal section of the entire patella, showing the union of the main fragments by fibrous tissue. There is a small bony fragment and a piece of hyaline cartilage enmeshed in the fibrous tissue forming the union. A small piece of hyaline cartilage is located on the articular surface of the proximal fragment. Fibrous tissue covers the articular surface of the distal fragment. The trabeculae of the proximal fragment are of average thickness and number, but the trabeculae of the distal fragment and interposed fragment are thin and scarce (×2.0).

Comment.—This is a good example of the result one should expect if a severely comminuted fracture of the patella is treated by immobilization. The fragments united by means of fibrous tissue and the articular surface became rough and irregular. Patellectomy increased motion 20 degrees and prevented the development of severe patellofemoral arthritis.

SUMMARY AND CONCLUSIONS

The clinical records of 42 patients with old and ununited fractures were studied. There were 38 ununited fractures and 4 symptomatic old united fractures. The results of the various methods of treatment were compared. Specimens from 15 cases of old or ununited fractures were studied grossly and microscopically. Three interesting cases which illustrate important clinical and pathologic findings were summarized and included.

Ununited fractures of the patella should be treated by total or partial excision. If the fracture is transverse, it is often possible to excise the smaller fragment and leave the larger fragment to reattach to the quadriceps or patellar tendon. Old ununited comminuted fractures of the patella should be treated by patellectomy.

Disabling traumatic arthritis of the patellofemoral joint resulting from fractures of the patella should be treated by patellectomy whether the original fracture has united or not.

Varying degrees of traumatic arthritis of the patellofemoral joint probably develops after all patellar fractures. Certainly, some degree of traumatic arthritis develops in all cases of old ununited fracture of the patella.

In our study the majority of specimens revealed degeneration and replacement of hyaline cartilage by fibrous tissue. These findings appeared to be a combination of cartilage degeneration plus the results of injury and repair.

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SOLITARY INTRATHORACIC NEUROFIBROMA

A Report of Two Unusual Cases

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INTRODUCTION

DURING the past decade, as mass roentgenography of the chest has become commonplace, increasing numbers of intrathoracic tumors are being detected and removed. Among them are certain solitary, benign neurogenic tumors (neurofibromas) which characteristically are situated in relationship to the posterior mediastinum. Recently, we observed two cases in which a tumor of this type was present at a most unusual site. Accordingly, we are reporting our cases and reviewing the literature briefly, in the hope that new interest will be aroused in the subject.

INCIDENCE

Intrathoracic neurogenic tumors, once considered to be quite rare, are being reported with increasing frequency. Thus, while Epstein[7] in 1937 was able to collect only twenty-four cases from the entire literature, we estimate that approximately 180 cases have been recorded to date. If our own past experience constitutes a criterion, a far greater number of such tumors have been encountered than reported.

CLASSIFICATION

The histogenesis of neurogenic tumors remains a subject of controversy, with the result that the terminology employed in the literature is not uniform. The vast majority of neurogenic intrathoracic tumors may be divided into two main groups. Group 1 includes those which arise from the nerve sheath; Group 2 consists of those which arise from the sympathetic nervous system.

Group 1.—Tumors comprising Group 1 are, for the most part, benign in nature. They may arise from spinal, cranial, or sympathetic nerves,[6] and are composed almost always of both neural and connective tissue. There is considerable dispute concerning the precise element of the nerve sheath that gives rise to these tumors. Certain pathologists state that the endoneurium and perineurium are the primary source, and that the lesions therefore are of mesodermal origin. These observers employ the descriptive terms "neurofibroma" and "perineural fibroblastoma." Another group of pathologists believes that tumors of Group 1 arise from the Schwann cells of the neurilemma and that, accordingly, they are of ectodermal origin. These men employ the terms "neurilemoma" and "Schwannoma." (Stout[25] recently stated that, at present, the consensus is that all benign nerve sheath tumors are of ectodermal origin.)

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The literature is likely to confuse the reader further, because certain authors do not differentiate between solitary benign nerve sheath tumors and tumors which constitute part of the widespread neurofibromatosis of von Recklinghausen's disease. Thus, Cutler and Gross[5] made no such distinction. On the other hand, Stout[25] offered certain pathologic and clinical criteria for separating the afore-mentioned lesions into two distinct categories.

Group 2.—Tumors comprising Group 2 arise from elements of the sympathetic nervous system. At times, a single tumor may be composed of more than one type of nerve cell.[21, 26] Also, as pointed out by Dugan and Blades,[6] the tumor may arise from the sheath of the sympathetic nerve giving rise to a neurofibroma or neurolemoma. Under certain circumstances, a tumor may be considered as of both sympathetic and nerve sheath origin.[13, 21] Thus, it becomes obvious that at times there may be some overlapping of cases in Groups 1 and 2. Fortunately, the precise origin of the tumors under discussion is of little practical significance.

Kent and associates,[15] after analyzing a large series of cases, reported that the differentiated, solitary, benign nerve sheath tumor (neurofibroma) was the most common type of intrathoracic neurogenic tumor, with the ganglioneuroma next in frequency. Silveus and Adams[22] are of the opinion that the neurofibroma is the most common benign mediastinal tumor. Our own analysis of the literature indicates that neurofibromas and ganglioneuromas have been reported in almost equal numbers.

INCIDENCE OF MALIGNANCY

Kent and co-workers[15] reported that, in 105 cases of intrathoracic neurogenic tumor of all types, 37 per cent were malignant. On the other hand, Maurer and associates[17] stated that only approximately 10 per cent of such lesions were malignant. Regarding sympathetic nerve tumors, malignancy depends upon the degree of cell maturity as is often the rule in other tumors arising from specialized tissues. Concerning nerve sheath tumors, Stout states that lesions of the solitary neurilemoma (neurofibroma) group are not malignant. In cases of multiple neurofibromatosis however, Hosoi[14] estimated that malignant transformation occurred in approximately 13 per cent. Cutler and Gross[5] believe that certain neurofibromas, which partake of the characteristics of both the neurofibroma and the neurogenic fibrosarcoma, may become malignant. Such lesions grow more rapidly than benign lesions and often recur locally following extirpation. They do not metastasize, however. From all of the foregoing, it is apparent that the incidence of malignancy in neurogenic tumors is significant and has an important bearing upon therapy.

LOCATION

The vast majority of intrathoracic neurogenic tumors arise from neural elements which lie within, or very close to, the posterior mediastinum. Thus Kent and associates,[15] in a series of 123 cases, found only four instances in which a solitary, benign neurofibroma was situated in the anterior mediastinum.

Occasionally, a neurofibroma may assume an hourglass or dumbbell shape, with part of the tumor lying within the posterior mediastinum and the remaining portion located in, or near, the spinal canal. Under such circumstances, the lesion may be assumed to have arisen from nerve elements which are situated within the mediastinum, the vertebral canal, or the intervertebral foramina.[12] Solitary, benign intrathoracic neurofibromas are very rarely found in the lateral portions of the chest and, in reviewing the literature, we were able to find reports of only two such cases.[5, 9] Accordingly, we are reporting another case of this type, the lesion being situated in the anterior axillary portion of the chest and arising from one of the intercostal nerves.

CASE REPORTS

CASE 1.—R. F., a 39-year-old white woman, was admitted to The Mount Sinai Hospital on Sept. 7, 1947, because of pain and the presence of a mass in the right chest of three months' duration. Three months previously, during the course of a periodic health survey, the mass was discovered on x-ray examination.

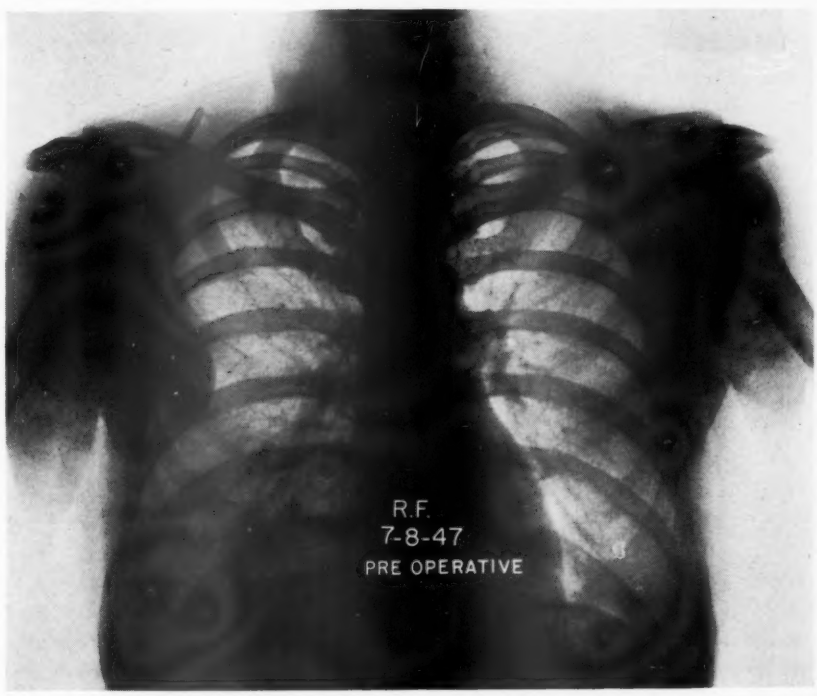

Fig. 1 (Case 1).—R. F., Posteroanterior film taken prior to operation. Note smooth ovoid lesion in axillary portion of right hemithorax.

Soon thereafter, the patient began to complain of mild intermittent discomfort in the substernal region and anterior portion of the right chest. This was associated with moderate tenderness on pressure in the latter area. There was no cough, dyspnea, or hemoptysis at any time during the illness. By the time the patient entered the hospital, the pain had begun to diminish in intensity. At no time had any constitutional symptoms been present. The past history and familial history were irrelevant.

X-ray examination in the posteroanterior position, performed approximately one month after onset of symptoms, disclosed an ovoid shadow in the axillary portion of the right hemithorax. The shadow extended from the level of the third to the fifth ribs (Fig. 1).

The shadow was well-defined, had smooth contours, and was of uniform density. When viewed in the left oblique position, it measured 2½ by 1½ inches in its vertical and transverse diameters, respectively. The appearance of the lesion suggested that it was of extrapulmonary origin and probably originated in the thoracic parietes. The ribs revealed no abnormalities (Fig. 2).

On physical examination, the patient appeared to be in excellent health. The only positive physical finding consisted of moderate tenderness anteriorly in the right axilla, in the general region of the fourth and fifth ribs, and intervening intercostal space. All laboratory findings were negative. The presumptive diagnosis was that of a benign tumor, probably arising from the pleura.

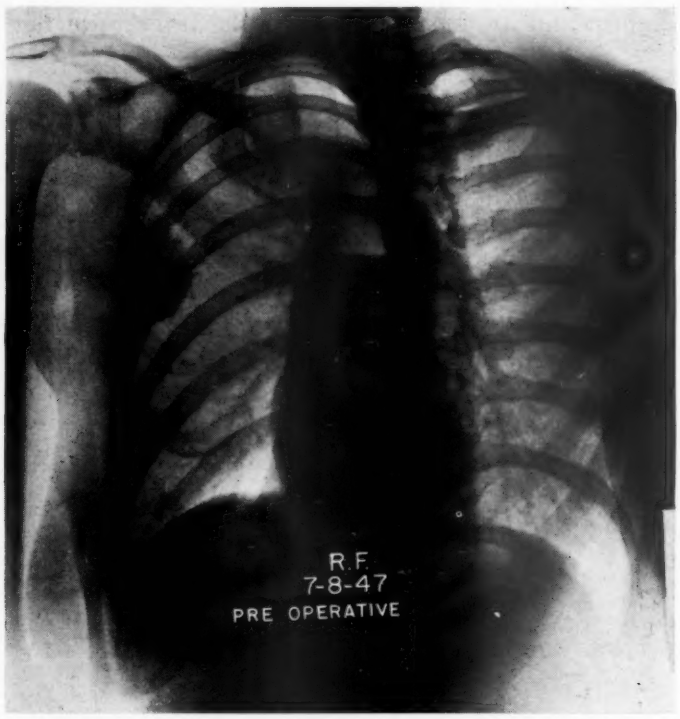

Fig. 2 (Case 1).—R. F., Left oblique film taken prior to operation. Note sharp delineation of tumor lying in anterior axillary region of right hemithorax. Tumor appears to originate in the thoracic parietes. The ribs appear normal.

On Sept. 8, 1947, thoracic exploration was performed by one of us (A. S. W. T.) under intratracheal, cyclopropane-oxygen anesthesia. A short incision was made high in the right axilla anteriorly, and the pleura entered through the third intercostal space. The lesion could not be palpated adequately, through the existing small intercostal incision; accordingly, the third rib was divided at the anterior and posterior extremities of the skin incision. The doubly divided rib then was retracted cephalad and the intrathoracic abnormality visualized. It was noted at once that the tumor was situated outside of the parietal pleura and lay in close proximity to the fourth rib. Although the tumor extended into the thorax it was completely covered by, and indented, the overlying parietal pleura. The latter could be stripped readily from the tumor. The mass was elastic and bluish-gray in color. Since it appeared to be intimately attached to the fourth rib, a four-inch segment of the latter was removed together with the attached mass. The doubly-divided third rib, which was still attached to the second intercostal muscle bundle, was replaced and immobilized with several sutures. Penicillin, 100,000 units, was instilled into the pleura, and the lung reinflated by positive pressure. The thoracic parietes were closed in layers. Silk technique was employed throughout. The pleura was not drained.

The postoperative course was uneventful, the patient being discharged from the hospital on the seventh postoperative day with a well-healed incision. At the time of discharge, she was symptom-free. A small collection of fluid which was present at the right base, resorbed spontaneously.

Pathologic report of the surgical specimen was as follows: The specimen consisted of a resected portion of rib measuring 8.5 cm. in length, with a roughly oval-shaped cystic mass attached to its inner aspect. The mass measured 7 by 4 by 3 cm. It was completely encapsulated and could be dissected away from the rib, to which it was attached by fibrous tissue. The surface of the mass was smooth, and in places was bluish in color. Blood-stained fluid could be aspirated from the interior. There was no destruction of the rib. The intercostal nerve could not be identified. The microscopic diagnosis was "neurofibroma."

Fig. 3 (Case 1).—R. F., Posteroanterior film taken five weeks after operation. Note that tumor has been removed with a segment of the fourth rib. The third rib has been divided and replaced.

X-ray examination of the chest, performed five weeks after operation, revealed the right hemithorax to be clear (Fig. 3). During the two years since operation, the patient has remained well and several x-ray films of the chest have failed to disclose any evidence of recurrence of the tumor.

Our second case, one of solitary benign *intrapulmonary* neurofibroma, was even more unusual than the first. Tumors such as the one about to be described apparently are excessively rare. Bartlett and Adams[2] stated that numerous cases of neurofibroma of the lung, occurring in von Recklinghausen's disease, have been reported. However, a review of the references cited

revealed only one such case, and, in the afore-mentioned case, sarcomatous involvement of the lungs was found. Blum[24] reported a case of von Recklinghausen's disease in which the x-ray film disclosed an intrathoracic tumor which was assumed to lie within the lung. However, the patient was not subjected to operation and, accordingly, the diagnosis of intrapulmonary neurofibroma cannot be accepted without reservation.

Rubin and Aronson,[20] in 1940, described a case of neurofibromatosis limited to the lungs. In their case, multiple nodules were found in, and on the surfaces of, both lungs. The pathologic report of these nodules was "neurofibroma or perineural fibroblastoma." There was no evidence of generalized von Recklinghausen's disease. Bartlett and Adams[2] in 1946, published a case in which a solitary neurogenic tumor was found attached to the left main bronchus. The mass lay, for the most part, in the pleural space between the left upper and lower lobes. Pneumonectomy was performed, the tumor being reported a "neurinoma." Accordingly, the case which we are about to describe appears to be unique, in so far as it seems to be the only one in the literature in which a benign solitary neurogenic tumor has been reported to lie within the substance of the lung.

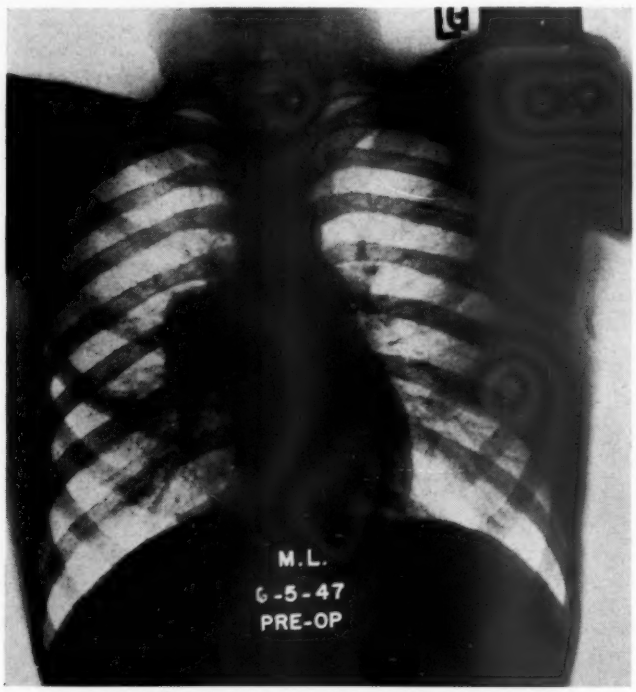

Fig. 4. (Case 2).—M. L., Posteroanterior film taken prior to operation. Note circumscribed shadow in right hilar region.

CASE 2.—M. L., an 18-year-old white man, was admitted to the Tumor Clinic of The Mount Sinai Hospital on June 3, 1947, a short time after a shadow had been discovered in the right side of the chest during the course of an Army pre-induction examination. Aside from mild dyspnea on exertion, he had no complaints referable to the chest. Neither cough, thoracic pain, nor hemoptysis ever had been noted. He had lost approximately twenty-five

pounds in weight during the eight months preceding admission, without obvious reason. The family history was entirely irrelevant. The past history was negative except for cerebral concussion, resulting from an automobile accident in April, 1945. Since the accident, the patient had suffered intermittently from headache and dizziness.

Physical examination disclosed a somewhat thin young man who did not appear acutely ill. The weight was 108 pounds. The only positive physical finding was slight, generalized lymphadenopathy. Temperature, pulse, and respirations were normal. All forms of laboratory examination were negative.

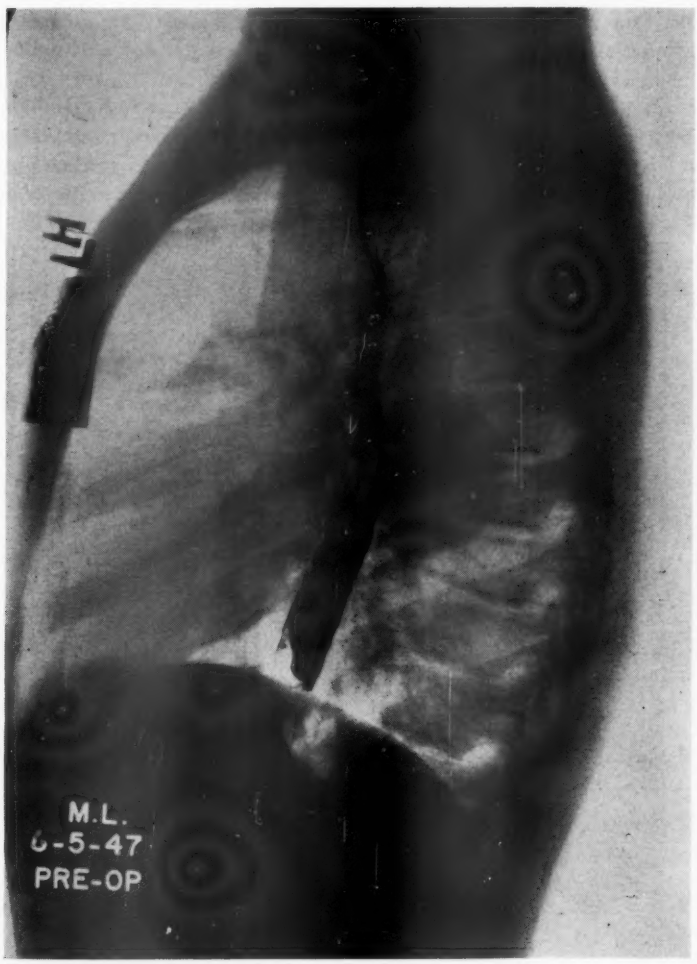

Fig. 5. (Case 2).—M. L., Lateral film taken prior to operation. Note smooth rounded tumor lying at junction of middle and posterior thirds of chest. (The typical position of a neurofibroma usually is further posteriorly.)

A posteroanterior roentgenogram of the chest made on June 5, 1947, revealed a circumscribed density measuring approximately 2 by 2 by 3 inches, in the mesial portion of the right hemithorax (hilar region) extending from the level of the sixth interspace to the eighth rib, posteriorly (Fig. 4). The roentgenogram, aside from the presence of moderate pulmonary vascular congestion on the right, was not remarkable. When viewed in the lateral position, the tumor appeared to be smooth, circumscribed, and rounded. It was situated at the junction of the middle and posterior thirds of the chest, and did not displace or encroach upon the barium-filled esophagus. It lay on a plane which, for the most

part, was anterior to the vertebral column (Fig. 5). (It was of particular interest to note that the shadow did not occupy the paravertebral gutter, the most common site of neurogenic tumors which arise from the sympathetic nerve chain.)

In the tumor clinic, the diagnosis of atypical mediastinal lymphoma was seriously considered and a therapeutic test of radiation therefore advised. Accordingly, a total of 1484 r. was administered between July 8 and 31, 1947. When this failed to influence the size and density of the mass, the patient was referred to the surgical service of the senior author for further treatment.

When admitted to the hospital, on Sept. 23, 1947, the patient stated that he had been suffering sharp pain in the region of the right nipple and mid-thoracic spine for three weeks. He added that the pain was increased by exercise and damp weather, but that the dyspnea of which he originally complained no longer was present. He also had regained eight pounds in weight.

Physical examination revealed the same slight generalized lymphadenopathy, which previously had been noted in the tumor clinic. A few coarse inspiratory rhonchi were noted posteriorly, near the angle of the right scapula. Slight postradiation pigmentation was present over the right breast. The remainder of the physical findings were noncontributory. All laboratory studies were normal.

Fig. 6 (Case 2).—M. L., Posteroanterior film taken approximately four months after operation. Note that tumor has been removed and is replaced by a fibrotic scar. The divided ends of the sixth rib have been replaced and wired.

On Oct. 1, 1947, operation was performed by one of us (A. S. W. T.). A right-sided posterolateral thoracic incision was made through the sixth intercostal space, after dividing the sixth rib close to the transverse process. When the pleura was opened, a mass was noted in the apical portion of the lower lobe. The upper and lower lobes were united by a few stringlike adhesions which were divided in order to permit the lobes to be separated. After this had been accomplished, and the interlobar (upper) surface of the lower lobe exposed, a firm grayish-white gentle swelling was noted projecting from the substance of the latter. The projection, which measured about 1½ inches in diameter and ½ inch in height, comprised the summit of a rounded mass which lay within the substance of the apical portion of the lobe alongside, and on a plane anterior to, the vertebral column.

The pleura over the summit of the tumor was incised and the mass progressively dissected out of the pulmonary parenchyma. The lesion was found to be sharply circumscribed and well encapsulated. After it had been removed, a few fine bronchial openings were noted in the tumor bed. Several small masses of fibrin foam were laid into the pulmonary defect, which then was closed with a series of interrupted mattress sutures of fine silk. After this had been completed, the defect in the lung was pleuralized with another tier of sutures, and 100,000 units of penicillin were instilled into the pleura. The residual air was removed from the pleura by catheter suction and the thoracic parietes were closed in layers, without drainage.

The postoperative course was uneventful, the patient being discharged on the twelfth postoperative day with a well-healed wound.

The pathologic report of the surgical specimen was as follows: The operative specimen consisted of a lemon-sized firm mass. The lesion was well encapsulated and of yellowish-gray color. Cut surface revealed a shiny grayish-yellow tissue, in which there were many streaks. Interspersed between these areas, there were many small yellowish softer areas. In places, the latter were nodular and linear. Microscopic diagnosis was "neurofibroma."

Fig. 7 (Case 2).—M. L., Posteroranterior film taken approximately one year after operation. Note reduction in extent of hilar scarring. No recurrence of tumor.

A film taken approximately four months after operation revealed the right hemithorax to be clear except for a few fibrotic streaks in the region formerly occupied by the tumor. The pulmonary vascular congestion was still present (Fig. 6). The patient was gaining weight and had no complaints referable to the chest. He was last observed on Sept. 21, 1948. At that time, he appeared in excellent general physical condition. His weight was 127 pounds and he was entirely symptom-free. An x-ray film, taken on Sept. 18, 1948 (approximately one year after operation) revealed the chest to be entirely normal and the pre-existing right-sided pulmonary vascular congestion to have disappeared (Fig. 7).

Comment.—It is to be noted that in both of our cases the presence of an intrathoracic mass was detected accidentally during the course of routine x-ray

examination. It also appears that whatever subjective symptoms were present did not commence until after the patients became aware that a tumor was present. Although the diagnosis of a benign tumor was made in each instance because of the sharp circumscription of the lesion, the precise nature of the growth was not known, or even suspected, until operation was performed. Had the tumors been situated in the characteristic paravertebral position, the correct diagnosis probably would have been made prior to operation. In Case 2, the presence of right-sided pulmonary vascular congestion, as a result of pressure of a pulmonary tumor on the return circulation of the lung, was of unusual interest.

Diagnosis.—The early diagnosis of benign intrathoracic neurogenic tumors is difficult because such lesions are likely to remain asymptomatic for a long period. Thus, in our two cases, it is impossible to state the duration of the lesions which were found at operation. Symptoms of mediastinal compression, such as are common in cases of anterior mediastinal tumor, are rare because the typical paravertebral site of the lesion permits the mass to expand freely into the pleural space and compress the lung rather than the structures within the mediastinum. Thus, mediastinal compression occurs only after the tumor has grown to an unusually large size.

It appears to be generally agreed that the most common subjective complaint is pain.[3, 5, 8, 15, 18, 21] The latter usually is dull and aching in character, and not uncommonly is of the "intercostal nerve" type. Pleural pain is stated to be rare.[21] Overholt and Souders,[18] and Harrington,[10] are of the opinion that pain becomes more marked when malignant degeneration occurs. Harrington also believes that the pain of malignant tumors is more severe at night than during the day. In the presence of an hourglass or dumbbell tumor, neurological symptoms may be the presenting or predominant clinical feature as a result of spinal cord or root compression.

Physical examination, as a rule, reveals no characteristic findings. Horner's syndrome or vocal cord paralysis may be present when the tumor is situated in the upper portion of the chest. Venous obstruction within the thorax occurs only when the tumor reaches unusually large size. The most important method of detecting these relatively asymptomatic tumors is by periodic roentgenography. Thus, Blades[3] reported that, of 109 cases of mediastinal tumor encountered in the Army, 94 were discovered on routine x-ray examination of the chest.

In the film, the typical benign intrathoracic neurogenic tumor appears as a round or ovoid sharply-circumscribed uniform density, which lies in the extreme posterior portion of the hemithorax close to the vertebral column (paravertebral gutter). (The rare exceptions to this location already have been discussed). With tumors of the hourglass or dumbbell type, pressure erosion of a vertebra may be noted in the region adjacent to the intervertebral foramen. Occasionally, areas of calcification may be present within the tumor.[21] When the lesion is lobulated or grows rapidly, malignancy must be seriously considered.[15]

Regarding differential diagnosis in typical cases, the other less common tumors to be considered are fibromas, chondromas, osteomas, myxomas, and remnants of the foregut.[4] Precise determination of the type of neurogenic tumor is extremely difficult, if not impossible, prior to operation.[3, 22, 23] Nerve sheath tumors and nerve cell tumors have similar roentgenographic characteristics and growth patterns. The age of the patient may be of assistance in arriving at a diagnosis for, in general, malignant undifferentiated sympathetic nerve tumors tend to occur in infancy, ganglioneuromas in childhood, and nerve sheath tumors in adult life.[23]

Therapy.—All authors are in agreement that the only treatment of intrathoracic neurogenic tumors is surgical removal as soon as the lesion is discovered.[1, 4, 5, 11, 15, 16, 19, 21, 23] Even if no symptoms are present, operative treatment is indicated because of the presence of malignancy or the danger of later development of malignancy.[4, 23] Furthermore, the diagnosis of malignancy is sufficiently difficult and the incidence of malignancy sufficiently high to warrant operation without delay. Then again, as the lesions enlarge they may produce pressure symptoms and become increasingly difficult to remove. Finally, the danger of operation is small, in the hands of those with experience in thoracic surgery. Thus, Blades reported that there were no deaths attributable to exploration in 114 cases of mediastinal tumor, operated upon in the Army.

It is agreed that radiation is of little or no value in the treatment of benign neurogenic tumors. Even malignant growths of such origin are little affected, and knowledge of this fact has led to the use of radiation therapy as a diagnostic test in cases in which a lymphoma is suspected. A dose of 1,000-1,500 r. delivered over the center of the mass should produce regression of a lymphoma within one month. If such change does not occur, the diagnosis of lymphoma should be discarded immediately and operation performed, as in our case of intrapulmonary neurogenic tumor (Case 2).

SUMMARY

Two cases of solitary benign intrathoracic nerve sheath tumor (neurofibroma), in which the lesions were atypically situated, are reported.

In the first case, the tumor was situated in the right anterior axilla and was derived from the fourth intercostal nerve; in the second instance, the lesion was found imbedded in the apical portion of the right lower lobe. Both cases constitute rarities in the literature.

In each instance, the lesion was discovered accidentally during routine roentgenographic examination of the chest.

The general subject of benign intrathoracic neurogenic tumors, including diagnosis and treatment, is reviewed.

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WOUND HEALING AND HEPARIN, USING HEPARIN DEPOSITS

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IT IS generally assumed that the first union of approximated wound surfaces is by fibrin from plasma or blood. It is believed that fibrin forms a scaffold for the formation of uniting fibroblastic growth, and that, therefore, the function of the fibrin clot is important for healing.[1] The next step consists in the bridging of the gap between the wound surfaces by histiocytes and capillaries. The fibrin clot between the surfaces of the wounds probably disappears either by lysis or by macrophages. Administration of anticoagulants would seem, therefore, to be able to prohibit the primary union of wounds, and the absence of a network of fibrin between wound surfaces might delay secondary healing. Yet, experimental results on the effect of anticoagulants on the healing process are controversial. Murray and Best[2] found no inhibition of healing of incisions in blood vessels by heparin. Lehman and Boys[3] reported on the prevention of peritoneal adhesions with heparin. In our own work, interrupted by World War II, we did not observe inhibition of healing by heparin. Our results were confirmed and reported by others.[4] Alrich and Lehman[1] found that tensile strength of wounds in heparinized rabbits was less than in nonheparinized control animals. They remarked, however, that twice as many heparinized than nonheparinized rabbits died and that this mortality may have introduced a selective factor into their experiments. Heparin has been reported to depress growth of tumor cells and of embryonic cells in tissue culture.[5-7]

Our interest in possible effects of anticoagulants on wound healing was aroused by an observation in 1941 on a heparinized male patient with complete disruption of an inguinal herniorrhaphy wound three days after operation. The edges of the wound showed no indication of healing. Blood clotting time was between 15 and 20 minutes, when disruption of the wound occurred. Although similar incidents have been observed on nonheparinized patients, the seriousness of the problem impressed us sufficiently to undertake a study on the rat and the dog. This was interrupted by war service of one of us (R. M. B.) and was not completed until now. Since the effect of anticoagulants on healing is still controversial, and since our experiments have not been reported by ourselves, nor in any detail,[4] we are presenting them here. Furthermore, we have applied a technique of heparinizing animals with a heparin-benzidine salt depot, which simplified experiments so much that our experience may be useful to others.

Experiments on Depot Heparin.—A suspension of protamine-heparin* complex was found either ineffective or of unreliable action, confirming the work

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of Chargaff and Olson[8] and of Jaques and co-workers.[9] An attempt to form a procaine-heparin compound was unsuccessful. The benzidine-heparin salt described by Jaques and associates[9] was found to provide adequate heparinization in rats and dogs. The compound is used in the form of a fine precipitate which resembles that of protamine insulin. Aqueous benzidine HCl (a 5 per cent solution was used) precipitates heparin quantitatively. The precipitate is removed from the supernatant by centrifugation, washed with 0.5 per cent benzidine solution, re-centrifuged, washed, and finally suspended in isotonic saline solution, to make up a volume equal to that of the heparin solution used originally. Thus, 1 c.c. of the suspension contained 10 mg. (1000 units) of heparin. The suspension was injected subcutaneously in amounts of 8.3 mg. (⅚ c.c. per kilogram) of heparin per kilogram of body weight in the dog, and 5 mg. (0.5 c.c.) in the rat (average weight 350 Gm.). The injections did not produce sloughs or apparent pain in the animals. The heparin is liberated slowly from the compound, maintaining an elevated clotting time for up to 24 hours. For measuring clotting time, the method of Lee and White was employed.

Method for Measuring Wound Strength.—Adult albino rats and mongrel dogs of both sexes were used. The animals were in a normal state of nutrition, and had normal total plasma protein and blood hemoglobin levels. Under sodium pentobarbital anesthesia, in a sterile operation, the abdomen was opened in the midline. The stomach was brought into the incision and a clean vertical cut was made through the entire thickness of the anterior wall of the prostomach in the rat and the fundus in the dog. The length of the incision was 1 cm. in the rat and 4 cm. in the dog. The incision was closed in the rat by six interrupted stitches through all layers of the stomach, using 0000 plain catgut. The abdomen was closed in two layers, and the skin wound was covered with iodine collodion. In the dog, the stomach was closed by eight interrupted stitches and by a Lembert serosal suture, and the abdomen was closed in three layers. Catgut was used for all sutures except those of the skin, where cotton was employed. The heparin-benzidine complex suspension was injected immediately after operation. The animals received one subcutaneous injection in the morning and another one at night. Repeated tests of blood clotting time were performed in the dogs in order to insure the presence of elevated clotting times throughout the duration of the experiment. In the rat, repeated withdrawal of blood was detrimental, and clotting times were determined at the termination of experiment only. However, intermediary clotting times taken on twelve control rats showed the presence of satisfactory 24 hours' heparinization. The animals recovered from the operation within 2 to 5 hours and were put back on the stock diets. After a number of days, specified in the tables, they were sacrificed painlessly. The tensile strength of the wounds was determined by the method of Bartlett and associates.[10] The stomach was ligated tightly at the distal end of the pylorus, the esophagus was sectioned 2 cm. above the cardia, and a glass cannula was tied securely into it. Then the stomach was removed carefully. The cannula in the esophagus was connected to a system consisting of rubber tubes, a T tube, a

mercury manometer, and a pressure bulb. The stomach was placed under water and held down manually. Then, air was pumped slowly into the stomach, until the suture line gave and air bubbles escaped. The height of the mercury column at that moment was noted, and the breaking point was registered in millimeters of mercury. After a number of control experiments on nonheparinized rats, the fifth postoperative day was chosen as most favorable for our test. At this time approximately 50 per cent healing seemed to have occurred. In the dog, the sixth postoperative day was used for the pressure test.

In the experiments on dogs, in addition to the test on the stomach, the tensile strength of the abdominal wound was measured. The skin sutures were removed, and a glass cannula was tied securely in a small incision through the abdominal wall in the flank. The same method as used for the stomach of the rat was employed, and the pressure was noted at which separation of the tissues of the wound occurred. In most tests, the skin wound opened first and the fascial and peritoneal wounds second.

In view of the high cost of heparin, and in order also to investigate the effect of Dicumarol on wound strength, a number of experiments were carried out with that substance. Dicumarol* was administered by mouth in daily doses of 2.5 to 5 mg. per kilogram of body weight. Clotting and prothrombin times were checked daily. Both were elevated from 50 to several 100 per cent throughout the experimental period.

RESULTS

Table I shows that the breaking point of the gastrostomy wound in control rats is most uniform 5 days after operation and that from that point on the values are more scattered. Five days after operation, the average value of the breaking points of the gastrostomy wounds was the same in heparinized as in nonheparinized animals (Table II). A scattergram showed no significant difference between the distribution of the values of both groups. Clotting times in Table II were taken at the 5-day period; in the nonheparinized control rats clotting times were almost uniform at 3 minutes (Table I).

In the dog experiments, the 6 day period after gastrostomy was chosen as end point. One animal (Dog 9) received injections of heparin only, to keep his clotting time elevated throughout the 6 day postoperative period. The control clotting time was 3 minutes; during heparinization clotting times were determined twice daily. They varied between 7½ and 35 minutes, and at one determination only they had dropped to 2 minutes. In the morning and at noon $\frac{5}{6}$ c.c. of heparin per kilogram was administered subcutaneously and at night $\frac{5}{12}$ c.c. per kilogram subcutaneously. In the case of Dogs 10 and 11 the heparin-benzidine complex was injected, as indicated in Table IV.

It is seen from Table III that the strength of the gastric and abdominal wounds in the control animals (Dogs 1 to 8) and in the heparinized animals (Dogs 9 to 11) was within the same range. In Dog 11, the resistance of the gastric wound was at the lowest level of the controls. However, this animal had pneumonia, which may have affected healing.

*Kindly supplied by Dr. R. K. Richards of the Abbott Laboratories, North Chicago, Ill.

TABLE I. HEALING OF GASTROSTOMY WOUNDS IN NONHEPARINIZED RATS

RAT NO.	NUMBER OF DAYS	BREAKING POINT (IN MM. HG)
1	5	42
2	5	50
3	5	68
4	5	76
5	5	76
6	5	78
7	5	78
8	5	88
9	5	88
10	5	88
11	5	94
12	5	112
13	6	60
14	6.5	88
15	6.5	134
16	6.5	148
17	6.5	140
18	6.5	250+
19	7	136
20	8	110
21	8	110
22	8	124
23	8	170
24	8	250+
25	8	250+
26	8	250+
27	13	178

TABLE II. HEALING OF GASTROSTOMY WOUNDS IN HEPARINIZED AND NONHEPARINIZED RATS FIVE DAYS AFTER OPERATION

EXPERIMENT NO.	HEPARINIZED		NONHEPARINIZED
	CLOTTING TIME (IN MIN.)	BREAKING POINT (IN MM. HG)	BREAKING POINT (IN MM. HG)
1	12	10	42
2	15	55	50
3	15	68	68
4	17	68	76
5	21	76	76
6	17	84	78
7	18	88	78
8	20	94	88
9	18	98	88
10	19	104	88
11	20	132	94
			112
Average		80	78

The dogs that had received Dicumarol died or had to be sacrificed before the end of the 6 day period. All of them had serious pathologic findings, indicated in Table III, such as pneumonia, fatty infiltration of the liver, and hematomas. In a number of them, total plasma protein and albumin levels decreased considerably during the postoperative period. Yet, the tensile strength of the stomach wounds, between 40 and 70 mm. of Hg, 2 to 4 days postoperatively, can be considered to be quite sufficient to withstand any intragastric pressure.[11]

TABLE III. HEALING OF WOUNDS IN CONTROL DOGS AND IN DOGS WITH HEPARIN-BENZIDINE OR DICUMAROL

DOG NO.	SEX	WEIGHT (IN KG.)	DAYS AFTER GASTROSTOMY	DRUG USED	BREAKING POINT IN MM. HG			REMARKS
					SKIN	PERITONEUM AND FASCIA	STOMACH	
1	F	5.0	6	None			80	
2	M	9.0	6	None			80	
3	F	6.4	6	None	180[a]	190	80	[a]Lower end of skin incision infected
4	F	10.4	6	None		200[b]	75	[b]Skin wound, slight infection
5	M	6.2	7	None		+300	160	
6	F	5.0	6	None		165	65	
7	M	8.0	6	None		280	75	
8	M	4.2	6	None		120[c]	70	[c]Skin wound, incomplete healing
9	M	7.3	6	Heparin only		140	170	
10	F	7.6	6	Heparin-benzidine		210[d]	140	[d]Skin wound infected
11	F	8.0	6	Heparin-benzidine	220	+220	50	Pneumonia
12	M	5.4	3(died)	Dicumarol			50	1 cm. of abdominal wound opened, yellow liver, pneumonia
13		5.8	4	Dicumarol			40	Hemorrhage, from abdominal wound, subcutaneous hemorrhage, bronchopneumonia, liver pale
14		4.6	3(died)	Dicumarol	200	60	60	Liver yellow
15		4.6	2(died)	Dicumarol			70	Subcutaneous hematoma, liver yellow, bronchopneumonia

TABLE IV. THE EFFECT OF HEPARIN-BENZIDINE SALT ON BLOOD CLOTTING (IN MALE DOG WEIGHING 13 KILOGRAMS)

	TIME	INJECTION	CLOTTING TIME (IN MIN.)
11/ 5/1942			
A.M.	9:30		6
	9:40	Heparin-benzidine, subcutaneous, 5/6 c.c. per kg.	
	10:10		8
	10:40		12
	12:00		13
P.M.	5:00		+25
	9:00		17
	11:10	Heparin-benzidine, subcutaneous, 5/6 c.c. per kg.	
11/ 6/1942			
A.M.	9:10		11
	11:30		14
P.M.	3:15		10
	4:50		8

DISCUSSION

It appears from our results that, in the rat, heparinization during the healing period of a gastric incision does not diminish the strength of the wound as determined by our method. Likewise, in the dog, there was no evidence, in three animals receiving heavy doses of heparin, that healing of abdominal wounds and of the gastric incision were impaired.

The lack of diminution of wound strength in heparinized animals appears contradictory to the known facts about inhibition of fibrin formation by heparin. However, while the mechanism of blood clotting has been and is being studied extensively, we know little about the mechanism of fibrin formation on surfaces of wounds. Heparin may be destroyed or inactivated in wounds by coagulase from bacteria,[12] by proteins or heparinase,[13] or by substances which accelerate clotting (Ac globulin); such substances may be present in wounds in greater concentration than in the blood, and thus fibrin formation may be normal. On the other hand, the laying of a fibrin structure may not be essential in primary healing of wounds. Foote[14] has described the process of wound healing to consist in the multiplication of fibroblasts and a concomitant production of intercellular fibrils, which are distinct from fibrin, as proved by special stains. These fibrils form a network which becomes denser as collagen forms, ending in the production of scar tissue.

The use of heparin-benzidine complex, proposed by Jaques,[9] has been successful in our hands. One to two subcutaneous injections per 24 hours seem to be sufficient to prolong clotting of blood in the rat and in the dog above 50 per cent (Table IV). We do not propose the use of the heparin-benzidine salt in man because benzidine (bi-aniline) is suspected to be cancerogenic, although apparently only when it acts over prolonged periods of time.[15]

In the case of dogs receiving Dicumarol, the evidence that the healing process is not affected is not as clear as in the case of heparin. Three of the four dogs in this series died 2 to 3 days after the operation and Dicumarol treatment. The fourth animal had to be sacrificed on the fourth day. In view of the short period of time after operation, the wounds showed considerable strength, approaching the lower levels of the dogs in the heparin series (Dogs 6 and 7).

However, we have no controls without Dicumarol; we were discouraged to procure these, in view of the complications encountered in every Dicumarinized animal not only in the present experiments but also in another, larger series of dogs, in which the effect of Dicumarol of liver function was tested. In the latter work (unpublished) we had evidence that Dicumarol decreased liver function (phenolsulfalein excretion) in the absence of loss of blood by hemorrhage or hematoma. Also, the effects of Dicumarol are not as easily controlled as those of heparin. Secondary factors, like fever, may increase its anticoagulant effect very considerably.[16] Dicumarol appears to have more generalized effects than has heparin. It has been reported to affect capillary permeability, and we have seen fatty infiltration of the liver in animals in which autopsies had revealed absence of hemorrhage. In all animals under Dicumarol regime, the plasma protein levels dropped, the albumin always more than the globulin. Since these dogs lost appetite and weight, the lower plasma protein levels may have been due to this. Yet, we have the impression from two animals, who did not bleed, nor lose appetite or weight during Dicumarinization, but whose plasma albumins dropped, that Dicumarol affects albumin production in the liver directly.

SUMMARY AND CONCLUSIONS

Heparinization of rats and dogs following laparotomy and gastrostomy did not affect the strength of the healing wounds. The effects of Dicumarol on wound healing in the dog are doubtful, and the use of this drug appears to warrant more caution than the use of heparin.

The heparin-benzidine complex has been found practical for prolonged heparinization of rats and dogs.

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VARIATIONS OF THE THORACIC DUCT

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THE thoracic duct is a poorly known structure in the human body. Indeed, not all medical students have seen it nor observed its course upon the completion of their anatomy courses. Little has been written about it since the time of Hunter and Cruikshank about 1800. Those papers which have been written have been mainly descriptions of damage to the duct following trauma or observations made during thoracic surgery.

The philosophy of Galen as translated by William Cruikshank seems to have prevailed since the publication of his book in 1786.* Galen wrote, "There is a certain length to which we may carry our researches, but if we attempt to go beyond that, we shall soon convince ourselves, that we neither understand our own imbecility, nor the great ability of Him who made us."

The following observations were made at post-mortem examinations over a period of five years and since numerous variations from the classical descriptions were found it is deemed necessary that they be described.

METHODS

After the body has been opened by the usual Y shaped incision and the abdominal contents examined in situ the bowel is removed from the ligament of Treitz caudad. The costal cartilages are next cut through, and the thoracic viscera examined in situ. The position of the superior surface of the aortic arch is then determined in relation to the thoracic vertebral bodies. The large vessels to the neck are then ligated, severed, and the entire contents of the thorax and abdomen removed en bloc. The azygos veins are then opened and examined from behind. The thoracic duct is then found and dissected out, also from behind. The entire course, its branches, length, and diameter, may then be determined and related not only to adjacent soft tissue structures but also to the spinal column, by measuring first the duct and then the vertebral column, beginning from the reference point where the arch of the aorta was before removal from the body. The superior portion of the thoracic duct may be examined during the course of the neck dissection. The skin and subcutaneous tissues are reflected cephalad exposing the neck anteriorly at least to the larynx. The clavicles are freed from the attached muscles and fascia and reflected to either side so that dissection of the structures beneath them is easily done. Thus, the entire course of the thoracic duct and the receptaculum chyli become available for examination. Following this, the examination of the remaining structures is done from behind, insuring system continuity in the post-mortem examination.

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*Cruikshank, William: The Anatomy of the Absorbing Vessels of the Human Body, London, 1786.

In this study 1,081 cadavers were examined. Some examinations had to be made after arterial injections by the embalmer, but this did not affect our study appreciably. Of 1,081 cases, 386, or 35.6 per cent, were embalmed prior to examination.

FINDINGS

The length of the thoracic duct varied from 36 to 45 cm. as measured from the upper margin of the receptaculum chyli to its entrance into the subclavian vein. The beginning or upper boundary of the cisterna chyli was as the level of the twelfth dorsal vertebra in 111 cases, at the level of the first lumbar vertebra in 360 cases, and at the level of the second lumbar vertebra in 610 cases.

The thoracic duct in all 1,081 cases coursed through the aortic hiatus between the aorta and azygos vein. The site of crossing from right to left was at the level of the fifth thoracic vertebral body in 480 cases and at the level of the sixth thoracic vertebral body in 601 cases. It or its variations then entered the superior mediastinum on the left side behind the aortic arch and subclavian artery between the left side of the esophagus and left parietal pleura to the upper orifice of the thorax. Single ducts were found in 663, or 61.3 per cent, of the cases. Two or more branches of variable length were observed in 418, or 38.7 per cent, of the cases. The variations in length and number of branches are given in Table I.

The caliber of the single thoracic ducts found varied from 2 to 4 mm.; 421 cases were 2 mm. in diameter, 201 cases were 3 mm. in diameter, and 41 cases were 4 mm. in diameter. Below the level of the eighth dorsal vertebra the thoracic duct was always a single duct. Pathologic lesions were found in only fourteen cases, an incidence of 1.3 per cent, and these were all found between the sixth and eighth vertebral body levels. Nine of these were tuberculous lesions; one a fungus lesion in which the yeast was seen intracellulary but not identified by culture because of prior embalming; two were metastases from uterine carcinomas; two from rectal carcinomas, and one from extensive melanocarcinoma of the vulva.

The right thoracic duct was identifiable in sixty-one cases of the total and always joined the left thoracic duct between the second and third dorsal vertebra level.

From the upper orifice of the thorax the combined or main thoracic duct arched 3 to 5 cm. above the clavicle crossing anterior to the subclavian artery in 892, or in 92 per cent, of the cases and in the remainder it crossed posteriorly. It was always anterior to the vertebral artery and vein and the thyrocervical trunk, lying in front of the phrenic nerve and medial to the scalenus anterior muscle. The duct ended in the angle or within 1 cm. of the angle formed by the junction of the left subclavian and left internal jugular veins.

The position and number of valves observed in the course of the thoracic duct are markedly irregular and without any constancy except for a terminal valve, which may be found at any position in the last 1 cm. of the duct.

TABLE I. VARIATIONS IN THORACIC DUCT

VARIATION	NUMBER OF CASES
Bifurcated	
For One Vertebral Body Length:	
From 1st to 2nd thoracic	17
From 2nd to 3rd thoracic	20
From 3rd to 4th thoracic	21
From 4th to 5th thoracic	7
From 5th to 6th thoracic	3
From 6th to 7th thoracic	2
	70
For Two Vertebral Body Lengths:	
From 1st to 3rd thoracic	4
From 2nd to 4th thoracic	23
From 3rd to 5th thoracic	16
From 4th to 6th thoracic	11
From 5th to 7th thoracic	3
From 6th to 8th thoracic	1
	58
For Three Vertebral Body Lengths:	
From 1st to 4th thoracic	3
From 2nd to 5th thoracic	31
From 3rd to 6th thoracic	41
From 4th to 7th thoracic	7
From 5th to 8th thoracic	0
	82
For Four Vertebral Body Lengths:	
From 1st to 5th thoracic	7
From 2nd to 6th thoracic	29
From 3rd to 7th thoracic	4
From 4th to 8th thoracic	1
	41
For Five Vertebral Body Lengths:	
From 1st to 6th thoracic	6
From 2nd to 7th thoracic	8
From 3rd to 8th thoracic	1
	15
No Bifurcations of Greater Lengths Were Found.	
Three Branches	
None of Only One Vertebral Body Length Was Found	
For Two Vertebral Body Lengths:	
From 1st to 3rd thoracic	0
From 2nd to 4th thoracic	0
From 3rd to 5th thoracic	3
From 4th to 6th thoracic	4
From 5th to 7th thoracic	0
From 6th to 8th thoracic	0
	7
For Three Vertebral Body Lengths:	
From 1st to 4th thoracic	1
From 2nd to 5th thoracic	4
From 3rd to 6th thoracic	4
From 4th to 7th thoracic	6
From 5th to 8th thoracic	9
	24
For Four Vertebral Body Lengths:	
From 1st to 5th thoracic	7
From 2nd to 6th thoracic	13
From 3rd to 7th thoracic	9
From 4th to 8th thoracic	2
	35

TABLE I—CONT'D

VARIATION	NUMBER OF CASES
For Five Vertebral Body Lengths:	
From 1st to 6th thoracic	1
From 2nd to 7th thoracic	3
From 3rd to 8th thoracic	5
	9
Those With Three Branches of Longer Length (one of seven and two of six)	3
	3
Multiple Branches	
One Vertebral Body Length	0
Two Vertebral Body Lengths	6
Three Vertebral Body Lengths	11
Four Vertebral Body Lengths	19
Five Vertebral Body Lengths	31
Six Vertebral Body Lengths	7

SUMMARY

The course and variations of the thoracic duct as observed in 1,081 post-mortem examinations are described. There are many more variations than are commonly recognized. Pathologic findings were observed in only fourteen cases. The thoracic duct is always a single duct from the level of the eighth vertebral body to the cisterna chyli, which fact is of importance to thoracic surgeons particularly. The right thoracic duct is not easily demonstrable. Perhaps we have convinced ourselves "That we neither understand our own imbecility, nor the great ability of Him who made us."

NEW TECHNIQUE AND GUIDE FOR ANGIOSTOMY

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FREQUENTLY in investigative work it is desirable to obtain blood repeatedly from an internal vessel not accessible to the usual methods of venepuncture. Procurement of such blood has required either an operative approach, sacrifice, or previous operation to reroute a vessel near the body surface. The first two entail alteration of physiologic conditions as well as not allowing repeated determinations over a period of weeks or longer. The latter is often technically difficult or impossible. The purpose of this report is to describe a new type guide with which blood may be easily obtained from internal vessels many times over long periods during which time the animal has minimal physiologic alteration.

In 1935 London[5] prepared dogs and obtained blood from internal veins utilizing a two-stage procedure. The first stage consisted of production of chemical and mechanical trauma to the venous wall and perivenous tissue in order to produce fibrosis. Several weeks later at the second stage a guide or cannula was sutured to this fibrotic area. Since the inner or attached end was sutured to or near a vessel it was always possible that blood obtained was not from this intended vein but from another near by. Nevertheless the apparatus has been used successfully by various investigators. Fig. 1 shows this type apparatus as used in a one-stage procedure by Dent and Schilling.[1] Hamilton, Woodbury, and Vogt[3] have used another modification whereby the entire apparatus is buried beneath the skin surface, the distal end consisting of a base plate sutured to perivascular tissue. Harrison and Liebow[4] recently reported a buried polyethylene apparatus whose base is sutured to perivascular tissue. This has a polyethylene membrane across the distal end just at the vessel which is useful in fixing the penetrating needle in proper position and in acting as a tampon on the vessel wall when the needle is withdrawn.

These techniques have certain objectionable features. A guide which is not completely buried results in a sinus tract and infection about it. The externally protruding end necessitates added care of the animal. Even though the base plate of a guide is sutured securely near a vessel it may wander from the original site. Blood obtained via such an open ended tube may be from a different near-by vessel which the penetrating needle has entered. In order to overcome these objectionable features a new type apparatus was designed and tested. This essentially is a metal guide fitted about the vein and extending from it to the subcutaneous tissue, the whole being beneath the skin surface. There are no sutures to vascular or perivascular tissue.

APPARATUS

Initially a crude model was made with tin shears, pliers, file, and soldering iron, using a tin can, solder, and a No. 17 needle (through whose lumen a No. 20

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needle passes with ease). Since the result in one dog was excellent, the foreign body was well tolerated, and blood was obtained with ease as frequently as desired, the same materials were used further and plans to obtain Vitallium or tantalum guides were abandoned. The latter materials are less irritative to tissue but much more expensive. Fig. 2 shows actual measurements of a guide successfully used about the portal vein.

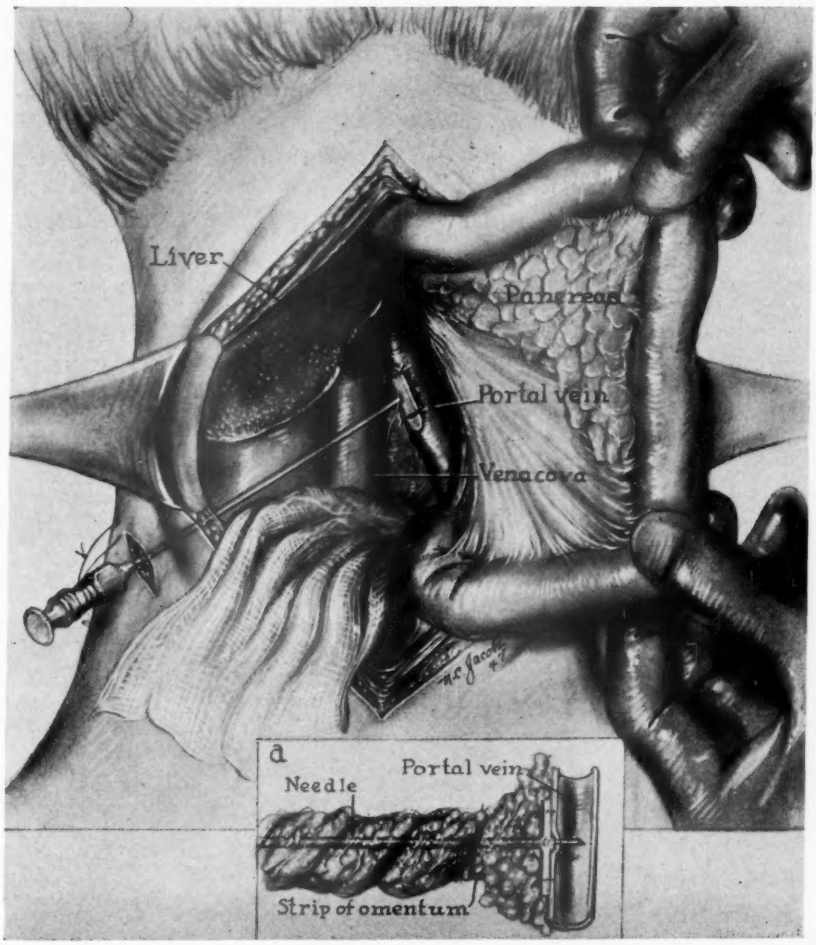

Fig. 1.—London type cannula sutured to portal vein. Inset *a* shows omental strip wrapped about this, with venepuncture needle protruding through the guide into the portal vein. (From Dent and Schilling,[1] Biochem. J., 1949.)

The needle was chosen for length and cut across squarely on the end. The rounded 5/8 circle end plate was then soldered to this by the projecting arm. The rounded 5/8 circle base plate then slid about this easily with a protruding arm to attach to the needle component by ligatures. Besides these ties, others about the ends of the enclosing base plate are tied so that a sturdy unit results.

PROCEDURE

Fig. 3 illustrates the guide in place about the portal vein projecting into the wound just prior to abdominal closure. In general the method of place-

ment was as follows. The operative approach was carried out on mongrel dogs under intravenous nembutal anesthesia supplemented by positive pressure machine oxygenation[2] when the chest was opened. The selected vein was gently dissected free for a sufficient distance to allow easy placement of the guide. Since several guides were available a selection was made prior to placement with particular regard to a natural position of the vein. The part of the guide with needle attached was initially placed after which the rounded base plate was slipped on and the two fixed together by ties as described. A site in the abdominal or chest wall was then selected on the basis of three criteria: (1) a position not in the operative wound, (2) a position which did not twist or kink the vein, and (3) a position where the head of the guide would be easily palpable and near a fixed landmark such as a rib or the wound scar itself. At this point

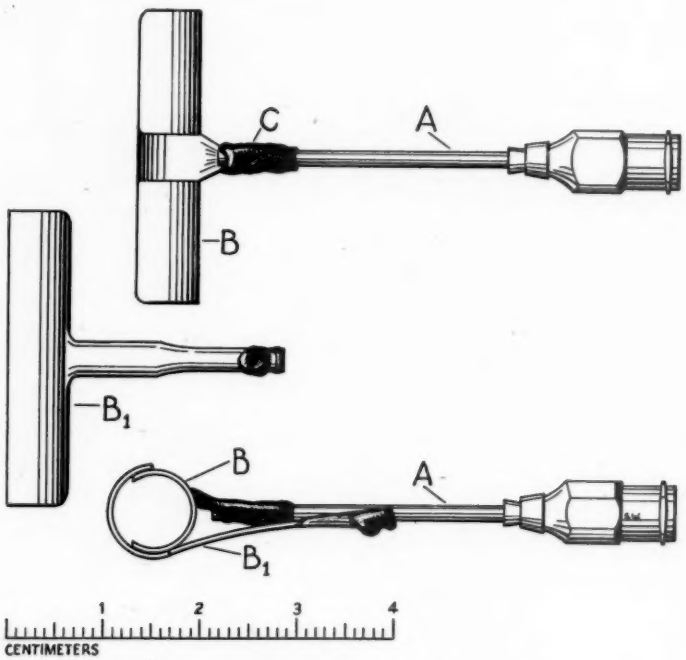

Fig. 2.—Specifications of sample guide for portal vein. *A* is a 17 gauge needle to which ⅝ circle tin with arm is soldered at *C*. B_1 is ⅝ circle tin end plate with arm. Lower drawing shows on-end view.

a small opening was made in the fascia and muscle and the head of the guide pushed through and fixed to the fascia by sutures from within so that the covering skin was never opened. The peritoneum or pleura was then closed about the guide with further sutures. In some instances it was feasible to dissect the skin-fat layer from the fascia, bring the guide out of the fascia under direct view, and replace the flap as the wound was closed. After two sinuses had occurred this was abandoned. At the conclusion the needle head was always easily palpable and in most instances an immediate venepuncture was done in order to view directly the result. Occasionally this showed the entering needle to slide off the vein to one side when the guide about it was too large and loosely fitting. In this case substitution of a better fitting guide remedied the difficulty.

The wound was lastly closed in anatomic layers with interrupted fine silk sutures.

During and after wound healing the head of the guide was always palpable. After location a No. 20 gauge needle with indwelling stylet was passed through the skin and into the hub of the guide. This was definitely indicated by the metallic grating which occurred. In order to assure that the entering needle passed into the guide and not down its outside, lateral bending of the entering needle in different directions was done as it was slowly introduced. Continuation of the metallic grating during this maneuver was indication of proper position. After this assurance the stylet was removed and with negative pressure from an attached syringe the venepuncture needle was slowly advanced into the guide until blood appeared or until the needle stopped when it reached the base plate. In case no blood was obtained the needle was withdrawn somewhat and the procedure repeated.

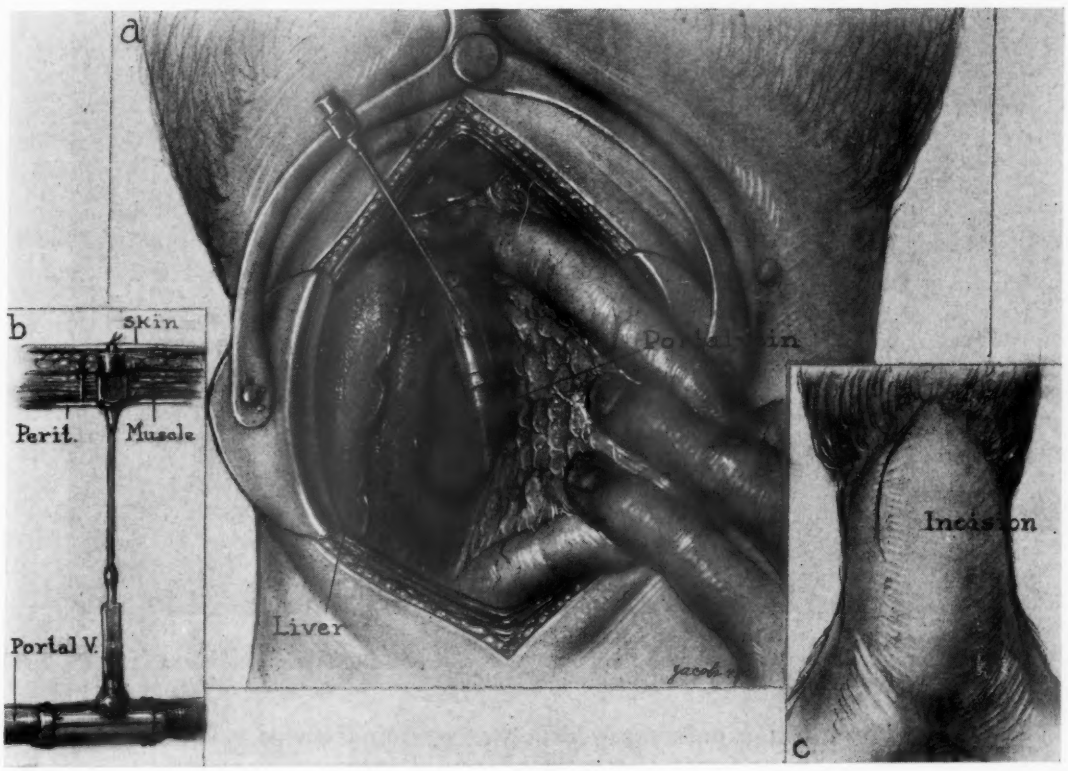

Fig. 3.—*A*, Guide in place about portal vein prior to closure of abdomen. Hand retracts duodenum and pancreas. *B*, Fixation of needle hub to fascia and peritoneum. Operative wound in skin was actually to one side rather than over this. *C*, Incision used.

RESULTS

Ten different guides were placed in four dogs, frequent venepunctures done, and autopsy examination made in each case.

Four *portal vein* guides were uniformly successful except for one in which the guide was too short and continued to retract into the deep tissues so that it could not be palpated. No venepuncture was ever attempted in this one. Fig.

4 shows 70 per cent Diodrast injected via a guide on the portal vein outlining the portal venous system. Ten to fifteen cubic centimeters of blood were always obtained with ease and venepunctures through the guides were done frequently and repeatedly, up to thirty-two times on a single vein. Two of the animals developed near-by sinuses which never interfered with venepuncture. No other complications occurred. The three successful preparations were carried two, three, and four months prior to autopsy examination.

The *vena cava* in its supradiaphragmatic portion was once prepared. This functioned well for thirteen days, at which time the dog was sacrificed. There was no complication.

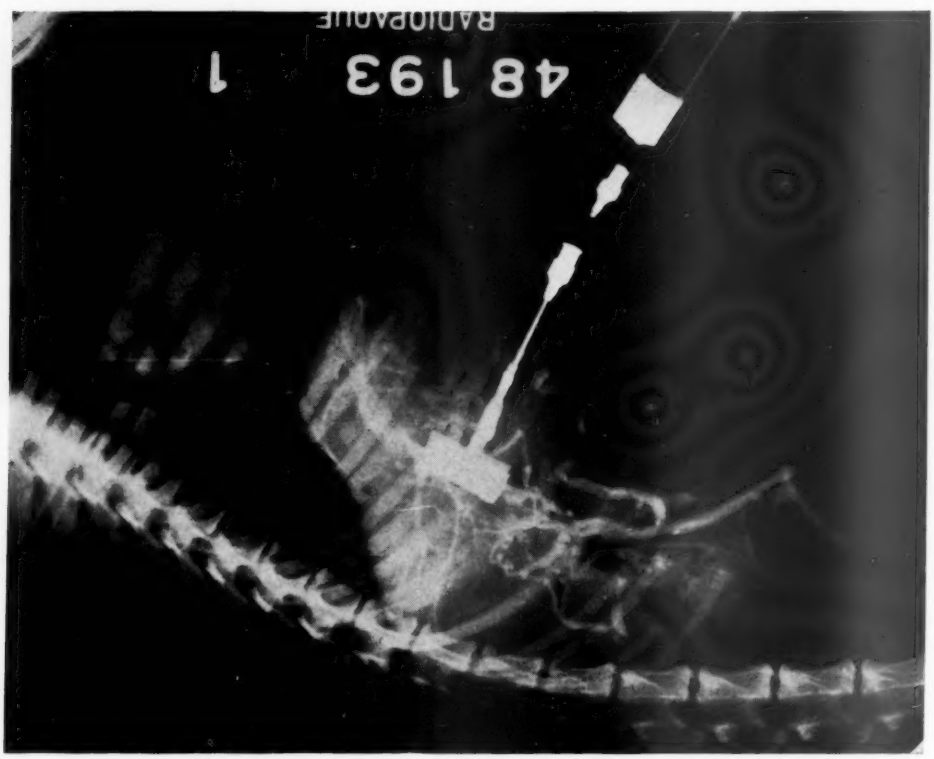

Fig. 4.—X-ray visualization of portal venous system of dog after 70 per cent Diodrast injection into the portal vein through guide. Visceral tributaries lie to the right. To the left are intrahepatic portal divisions and their ramifications.

The right inferior *pulmonary vein* was prepared twice. The first animal died of bilateral pneumonia after twenty-four hours and venepuncture was never attempted. The other functioned well and easily for twenty days after which function was absent and the animal died on the twenty-fourth postoperative day with massive pericardial effusion. This was presumably due to irritation by the foreign body which indented and pressed on the pericardium.

The *splenic, renal,* and *mesenteric veins* were all used once. Venepuncture of these smaller veins was never very easy. No more than a few drops to ½ c.c. of blood were ever obtained from them. No complications resulted from the procedures.

The three complications which developed were due to foreign body, consisting of the mentioned death of pericardial effusion and two sinuses of the abdominal wall. At no time was there evidence of bleeding upon withdrawal of the venepuncture needle from the vein. This was attributed to the firm fibrosis which developed about the guide and vein and to soft granulations which extended into the lumen portion of the guide.

At secondary operation or at autopsy the constant finding was a tough dense mass of adhesions about the metal, enclosing it in a fibrous sheath. Within the needle portion there were soft red friable granulations. Microscopic examination showed foreign body reaction and dense fibrosis. The enclosed vein was always thicker than usual with a tough whitish wall and decreased luminal size. Microscopically this apparently began as inflammation of the adventitia which spread through the wall with resultant scarring and fibrosis. Thrombosis occurred in the small veins only.

COMMENT

The following points are worthy of note:

1. If the animal can reach the projecting end of the guide with his teeth he is likely to tear the skin over it. A different point should be selected or a protective coat kept on the animal.

2. A guide too long is better than one too short. The short one retracts and may be lost, while the long one merely bulges the skin over it but is well tolerated beneath the freely movable skin.

CONCLUSION

A new apparatus and technique for procurement of internal venous blood is presented which is inexpensive, simply applied at a one-stage operation, and well tolerated for a considerable period by dogs.

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PRODUCTION OF LESIONS OF THE GASTRODUODENAL MUCOSA BY FREQUENT SHAM FEEDING

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SHAM feeding results in a high rate of gastric secretion by vagal stimulation. Hypersecretion is usually present in patients with duodenal ulcers. As one means of studying the importance of hypersecretion in the pathogenesis of peptic ulcers, it is reasonable to attempt to produce experimental ulcers by sham feeding.

The reports on attempts to produce peptic ulcers by sham feeding have been contradictory. For instance, Silbermann[1] found that 18 of 23 dogs developed ulcers of the stomach and duodenum after being sham fed three times a day for 14 to 49 days. Schmidt and Fogelson[2] repeated the experiment essentially as Silbermann had done. However, no ulcers or erosions were found in 5 dogs which were sham fed three times a day for 20 to 60 days. The findings of these and other authors are summarized in Table I.

In previous experiments sham feeding has been performed two or three times a day. It may be presumed that the stomach and duodenum were subjected to high levels of gastric secretion for only 2 or 3 hours with each sham feeding. Even then, the gastric juice may have been buffered by a meal introduced into the stomach. This does not simulate adequately the continuous secretion, particularly the night secretion, of duodenal ulcer patients. Gastric and duodenal ulcers can be produced in dogs by the continuous intragastric infusion of acid or acid and pepsin,[7, 8] but not by intermittent infusion.

The aim of this experiment was to expose the stomach and duodenum to relatively continuous hypersecretion by *frequent* sham feeding.

METHOD

Esophagostomies were produced in 16 dogs weighing 6.4 to 15.5 kilograms. The exteriorized esophagus was divided on the fifth postoperative day and the experiment begun 10 days to 3 months postoperatively. Sham feeding was performed 5 to 24 times a day. The sham-feeding diet consisted of a commercial dog food* or raw or cooked horse meat.

All animals were sacrificed when they refused to sham feed for 4 to 6 consecutive hours. The development of a gastroduodenal lesion was felt to be the cause of cessation of sham feeding. The interval of 4 to 6 hours was chosen to prevent a significant degree of healing of the lesions.[9]

Food was withheld from 9 intact dogs for 10 days although water was given ad lib. These dogs served as controls to determine the effect of starvation on the stomach and duodenum.

Several different schedules of sham feeding and real feeding were used. All dogs received intragastric water or 0.3 per cent saline solution. Nine received one daily intragastric feeding of a homogenized mixture of milk and commercial dog food. This is summarized in Table II.

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*Pard and Swift.

RESULTS

In the control group of 9 animals from which food was withheld for 10 days, no ulcers or erosions were found in the stomach or duodenum. The duodenum of 8 dogs was hyperemic (Table III).

TABLE I. PREVIOUS REPORTS ON THE PRODUCTION OF ULCERS BY SHAM FEEDING

AUTHOR	NO. OF DOGS	DURATION OF EXPERIMENT (DAYS)	SHAM FEEDING SCHEDULE	FEEDING	RESULTS
Panow[3]	8	--	--	--	1 perforating G.U. 3 perforating D.U.
Silbermann[1]	23*	14-49	3 times daily	--	18 ulcers of stomach and duodenum
Brenckman and White[4]	10	14-84	2 to 3 times daily	--	0 ulcers; some with gastritis and duodenitis
Buchner and Schneider[5]	11†	14	--	--	1 D.U. 3 with erosions
Puhl and Broderson[6]	6	3-14	--	--	0 ulcers; some with gastritis and duodenitis
Schmidt and Fogelson[2]	5	20-60	3 times daily	Once daily by stomach tube	0 ulcers; some developed duodenitis

*Five dogs sham fed poorly; sacrificed after 10 to 13 days and no abnormality noted.
†Four dogs sham fed poorly.

TABLE II. SCHEDULE OF EXPERIMENTAL PROCEDURES IN VARIOUS GROUPS OF SHAM-FED DOGS

NUMBER OF DOGS	SHAM FEEDING		DIET	RESULTS
	SCHEDULE	NUMBER OF DAYS		
5	Every hour for 5 min.	4 to 6½ days	None	Ulcer, 1; hemorrhagic erosion, 3; negative, 1*
2	Every 2 hr. for 10 min.	7½ days	None	Ulcer, 1; hemorrhagic erosion, 1
4	Every 2 hr. for 10 min.	4¼ to 8½ days	Once daily	Hemorrhagic erosion, 1; negative, 3
3	Five times daily, *ad lib*†	4 days	Once daily	Submucosal hemorrhage, 3
2	Five times daily, *ad lib*†	11 days	Once daily	Ulcer, 1; submucosal hemorrhage, 1

*Food entered stomach with each sham feeding.
†Allowed to sham feed until finished.

TABLE III. INCIDENCE OF LESIONS IN SHAM-FED DOGS AND FASTED CONTROLS

	TOTAL NO.	ULCER	HEMORRHAGIC EROSIONS	SUBMUCOSAL HEMORRHAGE	ESSENTIALLY NEGATIVE
Controls*	9	0	0	0	9
Frequent sham feeding	16	3	5	4	4

*Intact dogs, not fed for 10 days.

TABLE IV. CORRELATION OF AVIDITY OF SHAM FEEDING WITH LESIONS FOUND AT NECROPSY

AVIDITY OF SHAM FEEDING	NO. OF DOGS	LESION			
		ULCER	EROSION	SUBMUCOSAL HEMORRHAGE	NEGATIVE
Vigorous	6	3	1	0	2*
Fair	3	0	2	0	1
Poor	7	0	2	4	1

*One dog had food enter the stomach with each sham feeding and the other dog had more than 9 hours gastric retention of food.

Of 16 dogs which were sham fed frequently for 4 to 11 days, 3 developed acute peptic ulcers, 9 developed hemorrhagic erosions or submucosal hemorrhage in the stomach, and 4 had essentially normal gastroduodenal mucosa (Table III).

The acute ulcers were located at the pylorus, and the edges were overhanging (Fig. 1). Microscopically the ulcers penetrated the muscularis mucosa (Fig. 2). Hemorrhagic erosions appeared most frequently in the pyloric antrum (Fig. 3) although fundic erosions also occurred. Microscopically, these did not penetrate the muscularis mucosa.

Before necropsy was done on each animal, the over-all avidity of sham feeding was estimated. The avidity of sham feeding was correlated with the severity of the lesion found. The results are shown in Table IV. The most severe lesions were produced in animals which sham fed vigorously.

Fig. 1.—Acute peptic ulcer at the pylorus, produced by frequent sham feeding for 7 days. This lesion was 8 mm. in diameter.

Gastric acidity was determined at intervals following sham feeding in many dogs. When sham feeding was vigorous, the mean free gastric acidity at one hour was 88 mN units (range 48 to 132 mN), at 2 hours 81 mN (range 48 to 110 mN), and at 3 hours 50 mN (range 34 to 76 mN). When sham feeding was only fair the mean free gastric acidity at one hour was 36 mN (range 18 to 55 mN). When sham feeding was poor, the mean free gastric acidity at one hour was 28 mN (range 0 to 48 mN).

The results indicate that the buffering activity of food introduced into the stomach caused some decrease in the number of ulcers and other lesions, but not to a statistically significant degree. Nine dogs were fed through a

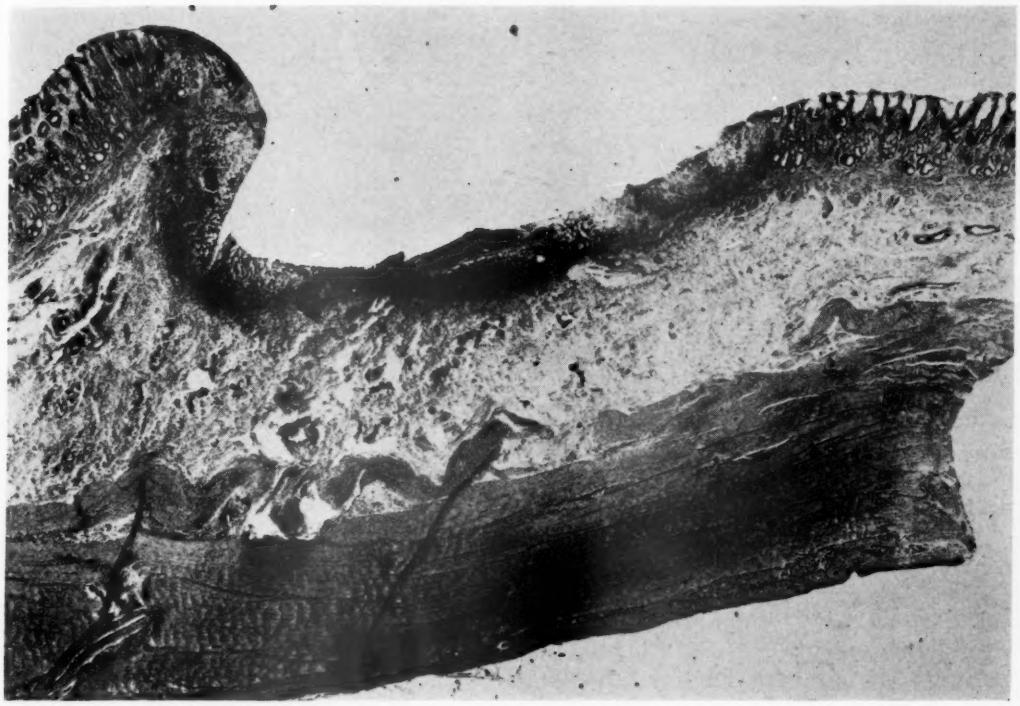

Fig. 2.—Photomicrograph of acute peptic ulcer shown in Fig. 1, demonstrating penetration of the muscularis mucosa and overhanging edge.

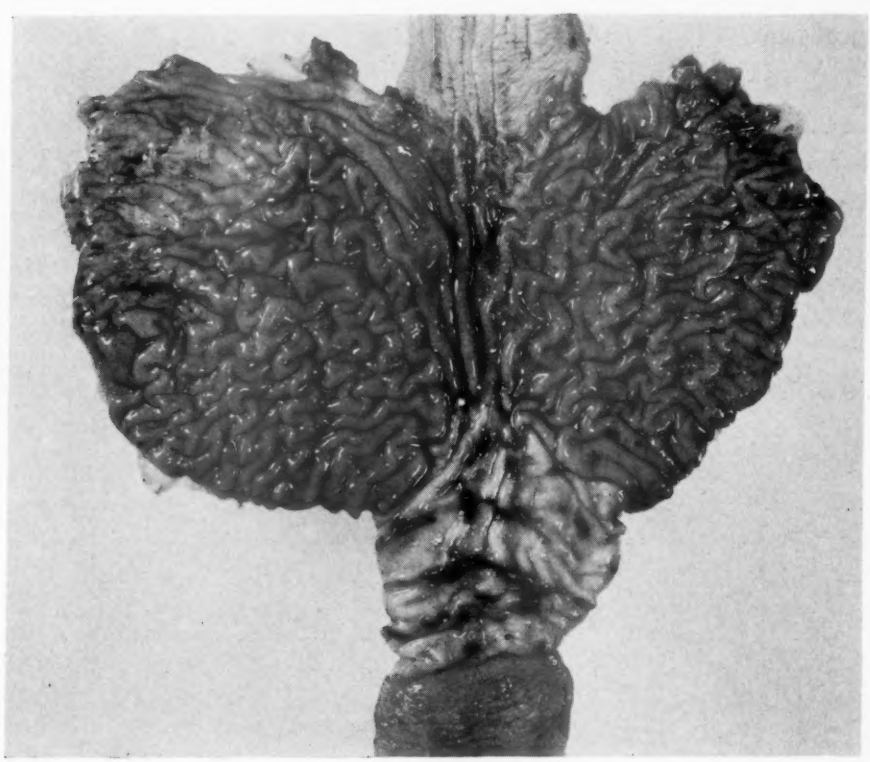

Fig. 3.—Acute hemorrhagic antral erosions produced by frequent sham feeding for 7 days.

stomach tube once daily. Six developed lesions of varying degree, of which one was an ulcer. Seven dogs were given only dilute saline solution. Six developed lesions of varying severity of which 2 were ulcers (Table II).

Peptic ulcers produced by sham feeding have been said to be the result of starvation.[2] However, no significant lesions developed in 9 control dogs which were starved for 10 days. In dogs which were sham fed, the percentage body weight loss was calculated from the preoperative weight and the necropsy weight. Dogs which developed no lesions had a mean body weight loss of 11.9 per cent (range 0 to 17.6 per cent). Dogs which developed submucosal hemorrhage had a mean body weight loss of 20.4 per cent (range 13.6 to 25.0 per cent). Dogs which developed hemorrhagic erosions had a mean body weight loss of 11.3 per cent (range 0 to 17.6 per cent). Dogs which developed ulcers had a mean body weight loss of 12.1 per cent (range 9.7 to 13.6 per cent). Starvation and malnutrition do not appear to be the primary factor in the production of peptic ulcers by sham feeding, but may play a role.

DISCUSSION

Prolonged, intense, continuous, physiologic vagal stimulation produced by sham feeding can, under the conditions of this experiment, lead to injury of the gastroduodenal mucosa. This suggests the possibility that similar factors may operate in the human peptic ulcer patient. However, despite claims to the contrary, the question of the existence of vagal hyperactivity in human ulcer patients cannot be considered to be settled. As we have pointed out elsewhere,[10] further evidence is needed. Therefore, the application of the findings of this study to the human disease must await further study.

SUMMARY

Continuous gastric hypersecretion in the dog has been produced by frequent sham feeding. Of 16 dogs, peptic ulcers developed in 3 and erosions or submucosal hemorrhages in 9 after 4 to 11 days of frequent sham feeding.

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A RESPIRATOR FOR USE IN INTRATHORACIC SURGERY IN THE DOG

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INTRODUCTION

DURING the past three years we have been attempting various intrathoracic surgical procedures on the dog. Our first attempts were markedly handicapped by lack of satisfactory anesthesia. Deliberate, meticulous surgery was prevented by the difficulty in maintaining respiratory exchange with an opening in the pleura large enough for adequate exposure. We have developed a method and an apparatus which we believe eliminates this difficulty.

Quenu and Longuet[1] in 1896 described a method of encasing the head of a dog in a rubber sac, sealing it about the neck, and rhythmically compressing the sac in order to create a positive pressure. They used chloroform for an anesthetic agent. In the same year Tuffier and Hallion[2] described a method of blowing air into an intratracheal tube by means of a bellows. Matas[3] in 1899 described the Fell-O'Dwyer apparatus which was a bellows arrangement for insufflating the trachea. Murphy[4] in 1905 described "A Practical Apparatus For Use in Intrathoracic Operations." This apparatus consisted of a box into which the head of the animal and the hands of the anesthetist were introduced and sealed in with rubber cuffs. The anesthetist operated a foot pump which pumped air through an ether bottle and then into the box. Sauerbruch[5] in 1904 described a chamber in which the patient and operators were placed, a negative pressure being maintained within the chamber. The constant negative pressure was supposed to keep the lung of the patient constantly expanded. In 1909 Meltzer and Auer[6] described a method of continuous respiratory movements, which according to Cutler[7] superseded all previous methods of maintaining respiratory exchange in an animal with an open thoracotomy. As originally described, the method of Meltzer and Auer depended on placing in the trachea, through a tracheotomy, an intratracheal tube. The outside diameter of this tube was smaller than the lumen of the trachea. A continuous flow of air passed first through an ether bottle and then into the intratracheal tube. Pressure was maintained at 20 mm. of mercury. The essential point of the arrangement was that the air which was introduced into the intratracheal tube escaped around the tube and out through both the tracheotomy and the larynx. The Meltzer-Auer method was modified subsequently to employ laryngeal intubation rather than tracheotomy. Pierce[8] in 1923 described an "Artificial Respiration and Ether Apparatus for Use with Compressed Air." This apparatus intermittently interrupted a stream of air passing through an ether bottle by

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means of a compressed air motor operating a valve. Mautz[9] in 1939 described a mechanical respirator as an adjunct to anesthesia, and in 1940[10] described an improved apparatus which could be integrated with the common closed system gas anesthesia machines. This apparatus provided for rhythmical compression of a rebreathing bag connected to the patient and to the anesthesia machine. The rebreathing bag was contained in a transparent chamber into which compressed air was intermittently introduced. This apparatus is now commonly used in human thoracic surgery.

The Meltzer-Auer method in our hands was unsatisfactory for the type of surgery we wanted to do. We found it difficult to maintain a proper depth of anesthesia, respiratory struggling was marked, and death of the animal frequently resulted. The apparatus described by Pierce was also unsatisfactory in our hands. With this apparatus a trained anesthetist was unable to maintain surgical anesthesia without anoxemia. Surgery was necessarily hurried and the operator was constantly working against time. The Mautz respirator, although most satisfactory for human surgery, did not appear practical for use in the laboratory because of the amount of equipment required. Furthermore, we wanted some system which did not require the services of a trained anesthetist.

APPARATUS

Sodium pentobarbital, or nembutal, administered intravenously is a very satisfactory anesthetic agent in the dog. In abdominal surgery we have used it some 500 times with a mortality rate from anesthesia of under 3 per cent.[11] The deaths which did result were almost always from overdosage by an inexperienced technician. On the basis of this experience it seemed desirable to use nembutal as an anesthetic for thoracic surgery, and to construct a respirator,* the sole function of which would be to maintain respiratory exchange.

Fig. 1 shows a diagram of the respirator. An oxygen tank is equipped with an ordinary tent gauge calibrated for flow in liters per minute. The oxygen flows through the respirator to the outlet which is connected with an intratracheal catheter. The flow is interrupted 20 times per minute by a solenoid activated gas valve. The valve is operated by an electric timing motor. When the valve is closed the oxygen flowing into the respirator must escape through the outlet and into the intratracheal tube. When the valve is open, the oxygen flows directly through the line to the exhaust and is lost to the outside air. During this same phase, that is when the valve is open, expired air will escape from the lungs through the intratracheal tube and out the exhaust.

It should be noted that no provision is made for "suction" during the expiratory phases. Mautz[9, 10] has pointed out that suction is not a desirable function of a respirator.

The timing motor is a 110 volt, 60 cycle, A.C. motor with a gear reduction box. The essential feature of the timing motor is an exposed brass timing gear which revolves ten times per minute. The magnetic valve is wired in series with this gear, and the circuit is made and broken by means of a contact brush. Por-

*The respirator was designed and constructed in cooperation with Mr. John W. Armstrong of Rochester, N. Y.

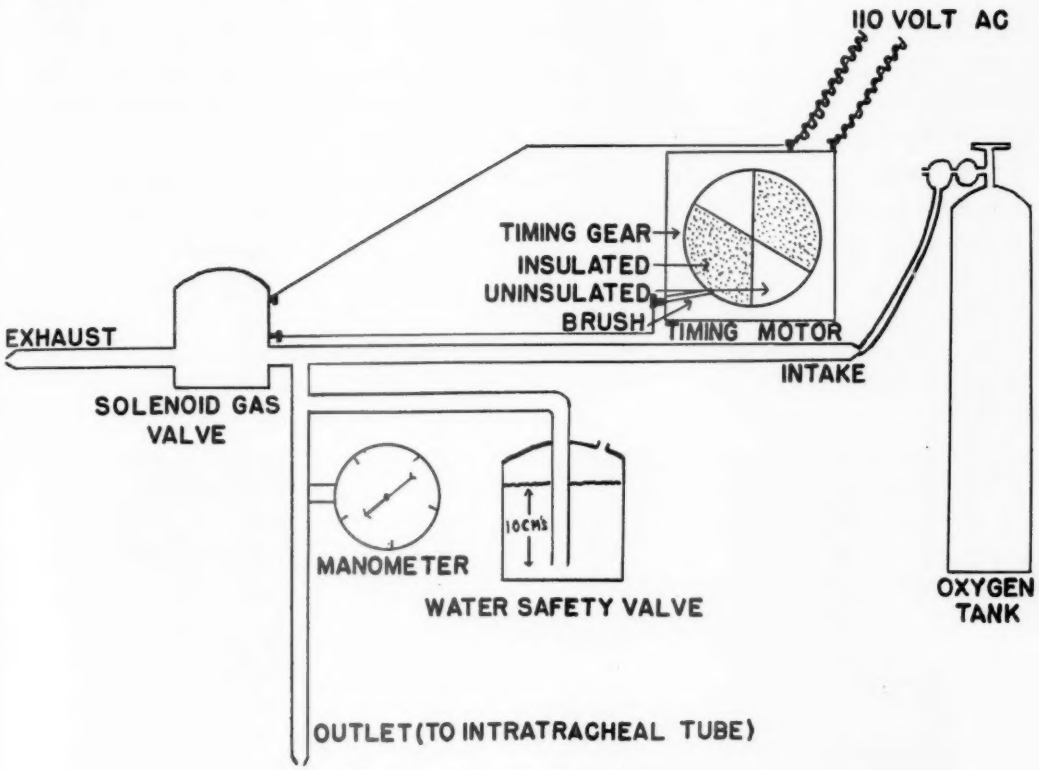

Fig. 1.—Diagram of respirator.

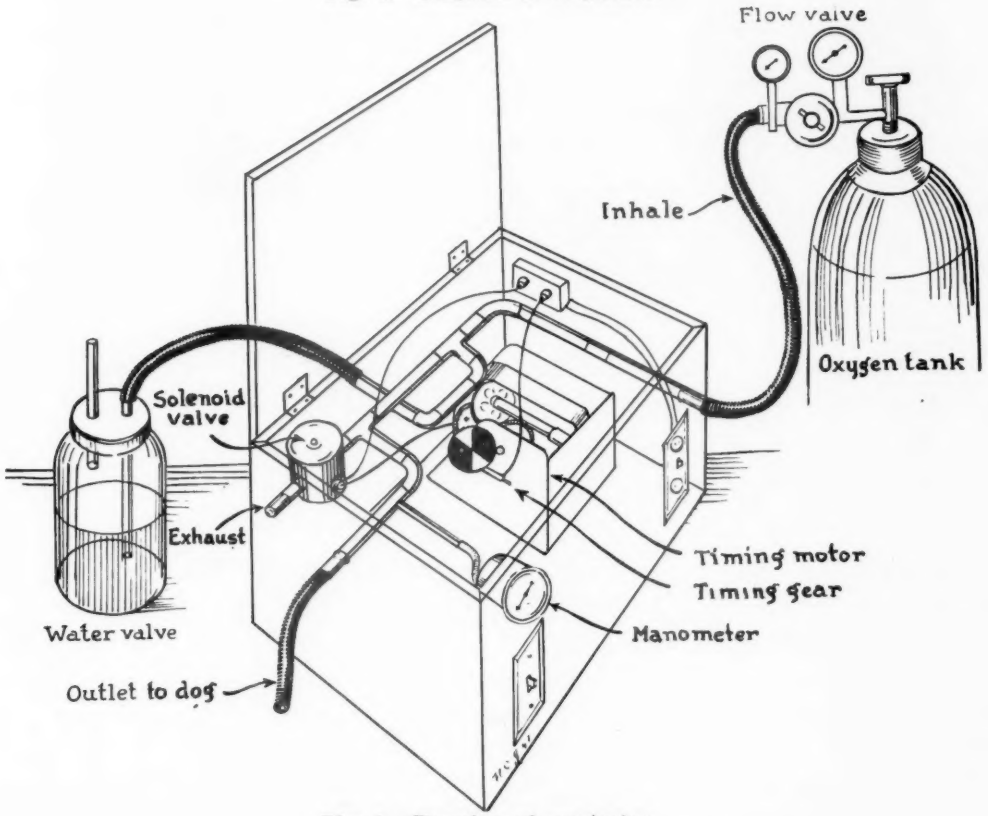

Fig. 2.—Drawing of respirator.

tions of the face of the gear are insulated in such a way that as the gear revolves, contact is made by the brush for one second and broken for two seconds. Making contact activates the solenoid in the valve and opens it. Breaking contact allows the valve to close.

We have used a maximum pressure within the system of 10 c.m. of water. A safety valve is incorporated in the respirator which blows off if a pressure higher than this is created. This safety valve consists of sidearm submerged to a depth of 10 c.m. in water. Pressures lower than this can be obtained by diminishing the rate of flow at the tent valve.

An aneroid manometer is incorporated in the respirator so that the pressure obtained at any given moment is visible.

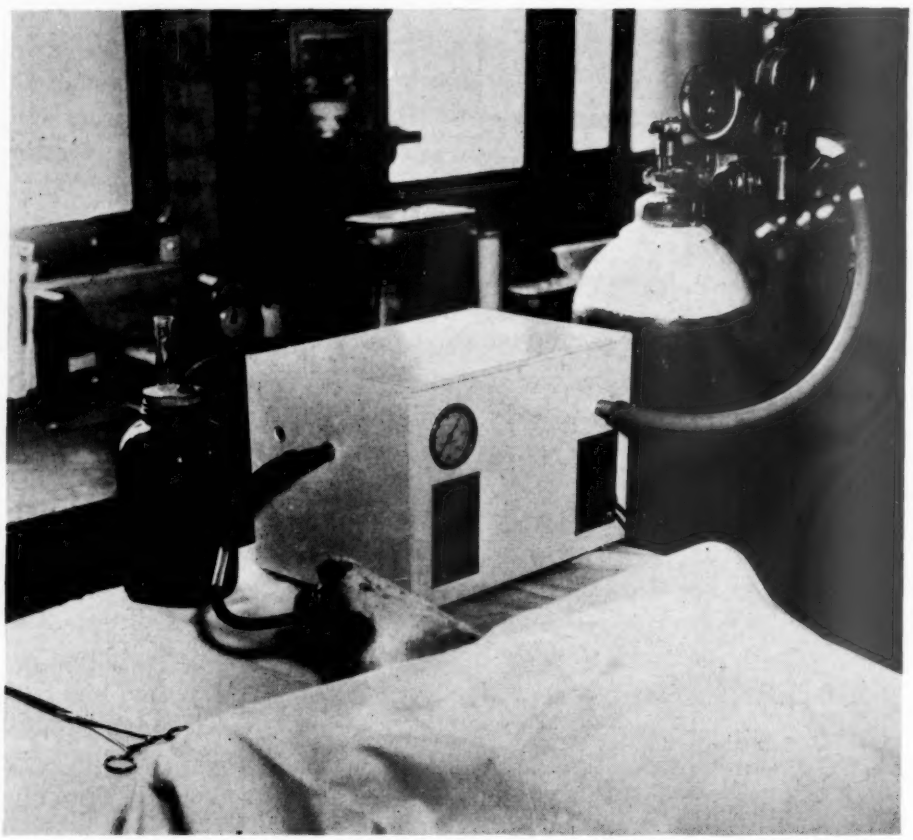

Fig. 3.—Photograph of respirator.

The respirator is constructed from easily available material. The tubing is ordinary one-half inch galvanized water pipe with ordinary plumbing T's and Ell's. The magnetic valve had been in use for several years on an automatic gas hot-water heater. The timing motor was one which was originally used to time the opening and closing of a steam radiator. The manometer was purchased commercially. The entire apparatus, with the exception of the safety valve, is enclosed in a wooden box 10 by 12 by 14 inches.

METHOD OF OPERATION

The method of operation is quite simple. The dog is strapped supine on the operating table. A superficial vein in the hind leg is selected and a solution of nembutal containing 65 mg. per cubic centimeter is injected. In general, 32 mg. per kilogram of body weight is required but there is wide individual variation from this in either direction. Our technique is to inject very slowly until the reflexes are lost and the respirations are slow and regular. We then stop the injection and give no more until indicated. When surgical anesthesia has been obtained, the needle in the vein is connected to a constant drip of Ringer's solution. A No. 24 Foley catheter with the blind end cut off is then put in the trachea and the bulb inflated. Intubation of the dog's trachea is simple. Extension of the head and traction on the tongue yields a clear view of the epiglottis. When the epiglottis is lifted, the vocal cords are exposed and the catheter can be slipped in without difficulty. The dog is placed in the desired position for surgery and the operation started. Just before the pleura is to be opened, the intratracheal tube is connected to the respirator and the oxygen flow started.

Fig. 2 is an artist's drawing of the apparatus. Fig. 3 is a photograph of the apparatus in use.

Sodium pentobarbital is a respiratory depressant. This seems to be an advantage when the respirator is used, since almost without exception, once the dog is on the respirator he makes no voluntary respiratory efforts. During a long operation additional nembutal must be injected. Indications for this are swallowing, struggling, or respiratory efforts. Recently we have been using Intocostrin in conjunction with the nembutal, and this may prove to be of value in accomplishing a smoother anesthesia.

RESULTS

Using the respirator, we have carried out open thoracotomies on over fifty dogs, resecting usually the seventh rib and opening the pleura wide enough to give adequate exposure. These thoracotomies have been done for lobectomy, division and re-anastomosis of the thoracic aorta, anastomosis of the subclavian artery to the pulmonary artery, and cannulation of the thoracic duct. The pleura has been open in these operations for an average of from two to three hours. We have kept the pleura open for as long as six hours in order to test the efficiency of the method and the apparatus. We have had no fatalities which we considered attributable to the anesthesia.

We have encountered no complications from the contact of the Foley bulb with the trachea, although it is realized that mild degrees of tracheitis would be difficult to recognize in a dog.

In all the operations the operator was able to dismiss anesthetic problems from his mind. He was able to carry out the surgical procedure with all the deliberateness that he desired.

The respirator is entirely automatic and will run for as long as is desired without attention. Additional pentobarbital can be injected when necessary by any laboratory technician acting as circulating nurse.

None of the dogs had more than minimal bronchial secretion. Bronchoscopy was carried out routinely at the close of each operation, but usually proved unnecessary. In two cases when the chest was closed and the respirator shut off, the animal did not breathe spontaneously. In each of these cases the dog was put back on the respirator with a 90 per cent oxygen—10 per cent CO_2 mixture for five minutes, and spontaneous respirations then began. In one case, satisfactory anesthesia could not be obtained with nembutal. When the initial dose was injected the dog developed shallow, jerking respirations which could not be eliminated. This dog later showed the same reaction when anesthetized with nembutal for an abdominal operation.

IMPROVEMENTS

Several improvements in the respirator are contemplated, and we are now constructing a model incorporating them. *One:* A three-way solenoid valve will be used to eliminate the waste of oxygen. *Two:* Sparking within the respirator will be eliminated by using a mercury tumbler switch tripped by a cam. *Three:* A smaller safety valve will be used, employing a commercial type diaphragm valve. *Four:* Adjustment of the respiratory rate and of the inspiration-expiration ratio will be made possible.

CONCLUSIONS

For intrathoracic surgery in the dog we have used intravenous nembutal for anesthesia. We have designed a simple respirator which is easily constructed from readily available material. In our hands the method has proved most satisfactory and is superior to any other method we have used. Improvements in the respirator will be made.

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COTTON AS SUTURE MATERIAL IN UROLOGIC SURGERY

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IN OUR graduate training in general surgery we had been taught silk technique and, of course, were convinced of its superiority over catgut in uncontaminated wounds. In urologic surgery, therefore, we used silk in operations upon the scrotal contents but feared to apply it to surgery of the urinary tract because troublesome silk suture granulomas were to be expected.

The medical literature is rife with articles on the disadvantages of catgut suture material which we may briefly summarize. Its rate of absorption is variable and is accelerated by infection and the presence of urine. Because of the inflammatory reaction which it incites in tissue, fibroplasia is delayed. When it is used in grossly contaminated wounds, close to 100 per cent of cases will develop infection. Since no wound is strictly "sterile," a significant number of "clean" wounds will become infected when the excessive inflammation caused by catgut develops. Because this is true, it is the rule for urologic surgeons to place drains in most wounds whether grossly contaminated or not. The use of drains can only increase the incidence of infection.

Since catgut has a low coefficient of friction, knots under tension are not secure and since this material is not pliable, knots cannot be brought down "tight." Catgut swells when buried in tissue and unless the ends of the sutures have been left long there is a tendency for these knots to untie spontaneously. This is particularly true if doubled catgut sutures are used. The tensile strength of catgut is lost rapidly and it is weak before adequate fibroplastic proliferation has developed. The only advantage that catgut could have over nonabsorbable sutures is the absence of troublesome sinus formation or foreign body granulomas. It is not uncommon, however, for catgut knots to be extruded from wounds a few weeks after their placement.

When the use of cotton sutures was popularized by Meade and Ochsner and others and evidence accumulated that sinuses and granulomas were rare or nonexistent when cotton was used, we decided to use it in operations upon the urinary tract. Cotton is easily sterilized. It excites little inflammatory reaction so fibroplasia appears early and progresses rapidly. It has been demonstrated that many contaminated wounds will heal without infection when fine cotton sutures are used. Clean wounds may be expected to heal per primam and therefore need not be drained. Cotton maintains its tensile strength well beyond the time that firm healing of the wound has taken place and because of its high coefficient of friction and its pliability, knots can be tied tightly and they will remain so. All authorities, however, stress the need for careful technique when cotton is used.

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The only disadvantage to the use of this material is the possibility that the buried cotton may act as a foreign body with the formation of sinuses or granulomas. First reports denied this but a few have recently appeared which admit of a number of late complications due to the cotton itself.

Two papers have appeared in the urologic literature which discuss experiences with cotton sutures and we have a personal communication from Nesbit concerning his results with this material. Bernardi and Macchi, in 1943, reported on the use of cotton sutures in forty-four patients. Twenty-one of these were aseptic operations applied to the scrotal contents. They noted that healing was excellent and that extrusion of cotton sutures was rare. Cotton sutures were also used in twenty-three wounds which they considered to be contaminated. These included such operations as prostatectomy, pyelolithotomy, nephrectomy, and drainage of abscesses. These authors were discouraged with the results in this group. Healing occurred by secondary intention and this took longer than if catgut had been used. Extrusion of cotton was the rule even months after the wounds were healed. They felt that cotton sutures, despite the claims of other authors, do harbor bacteria when bathed with infected urine and finally extrude themselves, and concluded that the use of cotton sutures is contraindicated in contaminated wounds.

In contradistinction to this, Melick in 1946 reported upon his experience with cotton in thirty-two cases. Drains were left in the wounds for as long as four days. He noted no complication whatever: no sinuses or extrusion of sutures, no induration of the wounds, no disruptions, and no hernias.

Nesbit employed cotton routinely some years ago and at first was much impressed by the uniformity of primary healing which he obtained. But, "after we had been employing cotton for a period of seven or eight months, patients began to return complaining of draining wound sinuses, and upon investigation it was found that a majority of these cases had healed per primam but after several weeks or months had developed small tender soft areas in the scar which eventually broke down. Cotton material extruded spontaneously from some; but in the majority the sinuses continued to drain until surgical removal was effected." This experience caused him to cease using cotton suture material.

Our series was started in April, 1942, and was closed at the end of 1946 in order to allow a minimum of two years for follow-up. Sharp dissection was used routinely at first but in 1943 we began to incise the lumbar muscles with the electrosurgical scalpel and to coagulate the smaller bleeders. Larger vessels were tied or transfixed with No. 40 or 60 cotton. The use of fine-pointed clamps, fine Ferguson and French-eye needles, light forceps, and the insistence upon careful hemostasis were stressed. Wounds were closed without drainage unless urine was expected to drain or gross contamination of the wound was present. Closure of muscles and fascia was accomplished with figure-of-eight doubled No. 40 cotton sutures. Interrupted No. 60 cotton sutures were used in the subcutaneous tissue and skin.

At the outset cotton sutures were used exclusively in all wounds except where they might penetrate the mucosa of the urinary tract. Here, 000 or 0000 plain catgut was used. Renal vascular pedicles clamped en masse were tied or

transfixed with double No. 1 chromic catgut rather than with cotton for fear the finer cotton might cut through the vessels.

This series is comprised of 196 cases and the majority of the patients were operated upon by eight members of the resident staff at the University Hospital. Of this group, 142 were classified as "clean"; 78 of these involved the upper urinary tract and included the removal of 53 kidneys, most of which were infected. They were "clean" because the pelvis or ureter was not opened (Table I). Complications in this uncontaminated group included five wound infections. Two developed following lumbar nephrectomy; one of these was mild and superficial while the other proved to be a deeply placed infected hematoma requiring surgical drainage. Of the fifteen nephrectomies performed through a transperitoneal approach, one became superficially infected following radiation therapy to the area and four cotton sutures were extruded spontaneously during the subsequent four weeks. The wound of one patient subjected to exploratory laparotomy discharged one cotton suture two months after operation though the wound healed per primam. A similar episode occurred following excision of a solitary cyst done through a lumbar incision. Six months later, a small but definite hernia could be demonstrated in this wound, though gross infection was never present. Following transperitoneal exploration and excision of a solitary cyst of the kidney, evisceration occurred in one instance and the wound was immediately closed with through-and-through silver wire sutures. No hernia developed nor were cotton stitches ever extruded. Only one mild wound infection developed following the operations upon the external genitals and this healed readily without complication.

Of the seventy-eight patients undergoing clean surgery of the upper urinary tract, then, only three, or 3.8 per cent, spontaneously discharged cotton from the wounds and two of these occurred late from incisions which seemed to have

TABLE I. UNCONTAMINATED WOUNDS

OPERATION	NUMBER	CLOSED WITHOUT DRAINAGE	WOUND INFECTIONS	COTTON EXTRUSION
Exploratory laparotomy	9	9		1 case, 1 knot at 2 months
Excision of solitary cyst, transperitoneal	2	0	1 Evisceration	
Division of horseshoe kidney	1	1		
Excision of solitary cyst, lumbar approach	3	0		1 case, 1 knot at 5 months
Nephropexy	7	7		
Adrenalectomy for cancer	1	1		
Nephrectomy, lumbar approach	38	33	1 Superficial 1 Deep	
Nephrectomy, transperitoneal	15	14	1 Superficial	1 case, for 1 month following x-ray
Ureterosigmoidostomy	2	2		
Varicocele	1	1		
Excision of lipoma of scrotum	1	1		
Amputation of penis	1	1		
Orchidectomy	13	13		
Repair hydrocele	20	19	1 Superficial	
Orchidopexy	28	28		
Totals	142	130	5	3

healed cleanly. Four (5 per cent) presented clinical evidence of wound infection and two of these were superficial. This experience compares quite favorably with that reported by the general surgeons.

Our experiences with cotton in contaminated cases have given quite different results. This group consisted of fifty-four patients whose wounds were either grossly contaminated or drained urine for varying periods (Table II). Thirty-five patients had operations upon the upper urinary tract and nine, or 26 per cent, of them extruded one or more pieces of cotton. A number of those in whom nephrectomy was done also had perinephric abscesses. One of these wounds discharged one knot two months after healing had taken place while another extruded one knot eighteen months after the operation. One patient of this group discharged four sutures over a period of four months followed by permanent healing. We cannot consider this an important complication for we feel that the use of cotton in these ten patients afforded quicker wound healing than would have been obtained had catgut been used.

The cotton sinuses which developed in the wounds of those patients subjected to conservative renal surgery were more troublesome. All extruded cotton for at least four months, while one persisted in this for eighteen months. In this group was the one granuloma, which caused the extrusion of much cotton for eighteen months. Surgical exploration demonstrated a large granulomatous mass which extended down to the peritoneum. It was completely excised and the wound was again closed with cotton sutures without drainage. It healed without infection and no further trouble ensued.

TABLE II. CONTAMINATED WOUNDS

OPERATION	NUMBER	COTTON EXTRUSION
Nephrectomy, lumbar approach	10	3 cases— 1 knot at 2 months, 1 knot at 18 months, 4 knots for 4 months
Nephrostomy	9	2 cases for 4 months
Pyeloplasty	4	1 case for 6 months
Nephrolithotomy	3	1 case for 18 months
Pyelolithotomy	3	1 granuloma excised
Ureterolithotomy	6	1 case, many knots for 6 months
Partial cystectomy	1	Many knots for 6 months
Diverticulectomy	1	
Suprapubic prostatectomy	4	1 case, many knots for 6 months
Vesicovaginal fistula	1	Many knots extruded into bladder
Cystostomy	6	1 case, few knots for 2 months
Epididymectomy, tuberculosis	6	1 case, few knots for 4 weeks
Totals	54	14

The sinuses which developed following operations upon the bladder and prostate were also quite bothersome, one persisting for six months. The complication following the repair of the vesicovaginal fistula was particularly interesting. Through a Cherney incision, the region of the left ureterovesical junction was exposed and the vaginal defect closed with interrupted sutures of No. 40 cotton. The opening in the bladder was closed with interrupted through-and-through sutures of No. 0 chromic catgut and this was re-enforced with Lembert sutures of No. 40 cotton which were placed superficially in the muscle only. The fistula was successfully closed but symptoms of cystitis persisted.

Cystoscopy one month after surgery showed the bladder to be normal. Two months later, re-examination demonstrated that two of the cotton sutures had migrated to a submucosal position; they were removed. During the next three months, four more cotton sutures were extruded through the mucosa after which vesical irritability ceased. We place no more cotton sutures in the detrusor muscle no matter how far removed from the mucosa. Epididymectomy was done six times for tuberculosis of that organ and, of these, one patient extruded four cotton sutures during the next four weeks, after which healing took place. These experiences explain why we gave up the use of cotton after one year of trial in cases where urinary drainage occurs. Not only did 25 per cent of them extrude cotton sutures but their sinuses were most persistent and quite troublesome to the patient. Only one, however, required surgical intervention for cure.

CONCLUSION

We have been pleased with cotton sutures in the type of case listed in Table I. Late complications from cotton have not been a problem and wound healing has been uniformly satisfactory. These wounds, furthermore, have been well tested by ambulation of the patient on the day after operation. The low incidence of wound infection is gratifying and though careful attention was given to technique, considerable credit for this must be given to the suture material itself. The use of cotton in contaminated wounds (Table II) was discouraging and we quickly gave it up.

Since this series was closed, we have been influenced by the experimental work of Hyde, who found that cotton was extruded from contaminated wounds only if the sutures were doubled or placed in a figure-of-eight manner. In the last three years, therefore, we have used interrupted single No. 30 cotton in place of the doubled No. 40 figure-of-eight sutures formerly used. One wonders whether this simple suture might not have decreased the late complications seen in the contaminated wounds.

SUMMARY

1. Cotton suture material was used in 196 urologic operations.

2. It proved to be a superior suture in wounds which do not drain urine. In this group, cotton sinuses and wound infections were rare. We are persisting in its use in these cases.

3. Of those wounds which drained urine, 26 per cent developed persistent and troublesome sinuses with extrusion of cotton and one of them required surgical excision of a granuloma. Catgut is the suture of choice for these wounds.

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JEJUNAL INTUSSUSCEPTION

Unusual Complication of the Use of the Miller-Abbott Tube

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DESPITE the extensive use of the Miller-Abbott tube or some one of the modifications thereof, serious complications are infrequent. Most of these are related either to the passage of the tube, or to pressure of the tube on structures in the upper respiratory tract or esophagus.[1, 2, 3] Relatively few serious incidents have resulted from passage of the tip of a long tube through the stomach and intestines, from the presence of the tube in the intestinal tract, or withdrawal of the tube therefrom.[4, 5, 6]

Intussusception producing intestinal obstruction with a Miller-Abbott tube in place must be extremely rare, judging by the paucity of such reports. Smith and Van Beuren[7] made the general statement that the intestine has been known to intussuscept itself upon the tube. Harris[8] cited an experience in which ileum intussuscepted into ileum due to an inflated Miller-Abbott tube balloon with death ensuing from an intestinal obstruction; and in a personal communication to Harris, N. J. Howard described a case requiring operation for intussusception due to a tremendously distended Miller-Abbott tube balloon. The only complete case report found in the available literature dealing with this type of accident was made by Warren and Cattell,[9] one of their cases of stenosis of the intestine terminating fatally with an intussusception and bowel perforation following intestinal intubation. It seems pertinent, therefore, to record an additional case in which intussusception with intestinal obstruction occurred immediately following the use of a Miller-Abbott tube, and in which it is believed that intussusception was related to the use of the tube.

CASE REPORT

A 55-year-old Negro woman was admitted to the Lankenau Hospital on Sept. 16, 1947, complaining of severe intermittent epigastric and periumbilical pain and repeated vomiting, both of twelve hours' duration. She had a normal bowel movement the day before admission, but no flatus nor stool had passed since then.

Previous operations included removal of a benign cervical polyp, a supracervical hysterectomy, right salpingo-oophorectomy, and an appendectomy on another admission.

Examination showed temperature 37° C., pulse 60, respiration 20, blood pressure 140/60. The patient was a well-developed and well-nourished woman, lying in bed, belching and vomiting bile-stained fluid. The abdomen was diffusely distended but there was neither rigidity nor muscle guarding. Lower abdominal tenderness was more pronounced on the right than the left. No masses were palpable. Peristaltic sounds were of normal pitch, but hypoactive. Pelvic examination was normal except for the cervical stump which was smooth to inspection, but tender on manipulation. Digital examination of the rectum elicited diffuse tenderness. The remainder of the examination was essentially within normal limits.

Routine laboratory work, including urinalysis of a catheter specimen, hemoglobin, blood urea nitrogen, icteric index, blood chlorides, and a smear of the cervix, was essentially normal. The leucocyte count was 13,400, of which 88 per cent were polymorphonuclear cells. A

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roentgenogram of the abdomen did not disclose calculi or distended loops of bowel. An electrocardiographic tracing was normal.

Initial management included continuous gastroduodenal drainage using a Levine tube with a Wangensteen suction apparatus attached, and the administration of parenteral fluids. From Sept. 17 to Sept. 19, 1947, the patient improved, remained afebrile, but had copious drainage through the tube. Enemas were returned clear and abdominal distention increased. Therefore, on Sept. 23, 1947, the Levine tube was replaced by a Miller-Abbott tube, the balloon of which was weighted with 2 c.c. of metallic mercury. Difficulty was encountered in passing the tip through the pylorus, but this was achieved on Sept. 26, 1947. After the balloon was injected with 30 c.c. air, it rapidly advanced to a point in the terminal ileum. Since the tip did not progress further, a thin barium suspension was injected through the tube, revealing on a roentgenogram an area of intestinal narrowing. The proximal loop was dilated, but some barium passed the constriction very slowly. On the basis of a near-total, mechanical obstruction of the ileum, operation was performed.

At the first operation, Sept. 30, 1947 (D.D.D.), abdominal exploration revealed the presence of calculi in the gall bladder. Numerous adhesions existed between peritoneum, omentum, and intestines, and the tip of the Miller-Abbott tube was located in the terminal ileum, 20 cm. proximal to the screen. Compromising the lumen of the bowel, immediately distal to the tip of the tube, was an obstructing cicatricial band which tightly bound the ileum at this point to a contiguous leaf of mesentery. The band was severed, the entire small intestine was freed of adhesions, and, after no further obstruction had been demonstrated, the wound was closed.

Twenty-four hours after operation, removal of the Miller-Abbott tube was begun at the rate of 10 cm. per thirty minutes. The balloon, which contained 30 c.c. of air, had been deflated and suction on the tube discontinued. The patient experienced crampy abdominal pain, and a greater drag was felt on the tube than is usual with its removal. The diet was increased to include soft items on the second postoperative day, and two enemas produced liquid returns containing fecal particles. Anorexia and vomiting on one occasion on the fourth postoperative day were thought to have followed a too rapid increase in the diet. The passage of flatus and two soft, brown stools from the eighth to the twelfth postoperative days permitted a sense of security concerning the patency of the intestinal tract. Nevertheless, the patient began to complain of "indigestion" and a sense of abdominal fullness. Anorexia was followed by vomiting, slight at first, but increasing within forty-eight hours to large amounts of bile-stained, nonstercoraceous fluid. The nature of the residual gastric contents suggested a high small intestinal obstruction. To confirm this, injection of a thin barium mixture through a Levine tube demonstrated roentgenologically dilatation of stomach and duodenum, with complete obstruction in an upper jejunal loop (Fig. 1). The patient having recently had a thorough abdominal exploration, the commoner causes of obstruction could reasonably be excluded. However, it was recalled that at laparotomy plication of small intestine over the Miller-Abbott tube was well demonstrated, and in fact a small incipient intussusception was noted. It was suspected in the light of these observations that the obstruction was due at this time to an intussusception in which the mesenteric vessels of the involved segment had not yet been compromised. The temperature, blood counts, and blood chemical evaluations remained within normal limits with appropriate supportive therapy, but the pulse rose to 100. On the fourteenth postoperative day the patient was again subjected to a laparotomy, with the end of a Levine tube in the stomach.

The second operation was done Sept. 14, 1947 (E. W. S.). As the peritoneal cavity was entered through an upper left rectus muscle-splitting incision, a dilated loop of small intestine immediately presented. The jejunum was traced from the ligament of Treitz for about 30 cm. where a firm, obstructing mass, an intussusception, was met. The intussusceptum was formed by 18 cm. of proximal jejunum which laid within the ensheathing layer of the intussuscepiens formed by the distal jejunum. Reduction of the intussusception was accomplished by very gentle traction and pulsion. The bowel wall was edematous but there was no unusual injection nor engorgement save at the neck of the process where moderate hyper-

emia was apparent. With reduction, several small tears were made in the boggy serosa. The mesenteric vessels were not thrombosed. A by-passing enteroenterostomy was established, a few pieces of gelatin sponge were placed over the few tiny serosal rents, and the abdomen was closed.

Two days following the second operation the patient was ambulatory, and on the third day she had a large spontaneous bowel movement. Gastroduodenal drainage was discontinued on the fourth day and the diet was gradually increased. Subsequent contrast roentgenograms showed slight dilatation of a jejunal loop, but free passage of the barium meal to the colon. The patient was discharged on the fifty-fourth hospital day, free of symptoms. On a follow-up visit in December, 1948, she was without complaints.

Fig. 1.—Roentgenogram after barium swallow, demonstrating high, upper jejunal obstruction.

Comment.—One might presume that the Miller-Abbott tube was instrumental in producing intussusception in this case. Multiple plications of the intestines on the long tube are usually seen when abdominal surgery is being performed upon intubated patients, as noted by McKittrick and Warren,[10] and even small transient intussusceptions must be common under these circumstances. The conditions necessary for establishing an intussusception which does not spontaneously reduce are not well defined, but one might conjecture that the same physiologic forces are at work which so commonly produce intussusception of the small intestine at the site of a tumor or polyp, the bulky end of the tube being physically analogous to a space-taking bowel lesion. Since the intussusception in this case was not a "reverse" type, it is inferred that the obstruction did not result from withdrawal of the tube. Furthermore, obstructive symptoms increased after the first operation, which suggests that the

intussusception developed with the Miller-Abbott tube in place rather than from its withdrawal.

SUMMARY

1. Serious complications resulting from the Miller-Abbott tube are relatively rare.

2. An unusual case of jejunal intussusception occurring with the use of the Miller-Abbott tube, requiring operative intervention and followed by recovery, is reported.

3. The mechanism for development of such a complication is obscure.

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AN ORIGINAL DRAINAGE CUP APPARATUS FOR ILEOSTOMIES AND FISTULAS

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INTRODUCTION

IN THE care of patients with ileostomies, particularly those with profuse watery discharge, the physician and nurse are beset with many problems: Among these may be included the prodigious nursing care necessary because of soilage; irritation, maceration, and erosion of the surrounding skin are almost invariable sequelae even after meticulous applications of metallic powders, pastes, resins, etc. designed to protect the skin. Since many of these patients are in a debilitated physical and mental state as a result of the pathologic condition demanding ileostomy, the added insults to the psyche from prolonged hospitalization and mounting expenses contribute incalculable anguish and retard convalescence. Thus it is evident that any apparatus which can afford some measure of relief to these patients is worthy of trial and use. The apparatus to be described was designed for the care of newly created ileostomies until such time that the dejecta become sufficiently formed to allow use of a suitable ileostomy bag. It has performed creditably not only in these cases but also in others (including cecostomies) with semisolid discharge; it has served satisfactorily in several cases of fistula of the small bowel and of the biliary tract; it should perform well with other types of fistula, for example, pancreatic, ureteral, vesical, etc.

DESCRIPTION AND OPERATION OF THE APPARATUS

Suction.—An efficient vacuum pump which delivers from three to eight inches (mercury) of negative pressure serves most satisfactorily. Although wall suction is suitable, the full negative pressure is not only unnecessary but also undesirable (to be discussed later in paper).

Cup (Fig. 1).—The Lucite cups are provided in three sizes: The smallest is adequate for a small ileostomy, whereas the largest is necessary for a double-barreled ileostomy or large fistula; in general, the intermediate size serves best for all-round purposes. In operation the cup is inverted so that the rim is directed toward the skin. A short sidearm tube, rigidly cemented into an opening just above the rim of the cup, provides prompt, dependent drainage of the confined discharge. A simple baffle over the roof of the cup is made possible by two discs of Lucite: The lower, with a wedge-shaped defect, is permanently cemented to the roof and gives vent to the beveled intake hole in the roof. The upper disc, slightly larger than the lower to prevent sheets, etc. from obstructing the entrance of air, is secured to the lower disc by means of two screws, one of which is permanently fixed and the other, detachable; by unfast-

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ening the latter, a knurl screw, the upper disc can be rotated on the lower and secured to it in either of two positions. In normal operation the eccentric opening in the upper disc is situated so that it does not communicate with the intake; this arrangement provides the baffle. On the other hand, if one desires to irrigate the cup or to provide exit for an indwelling catheter, the upper disc is rotated and fixed so that the eccentric opening overlies the intake.

The cups are transparent, light, and durable. Since Lucite becomes plastic above 180 F., the cups cannot be sterilized by heat; they can, however, be cleaned with warm, soapy water and sterilized with alcohol.

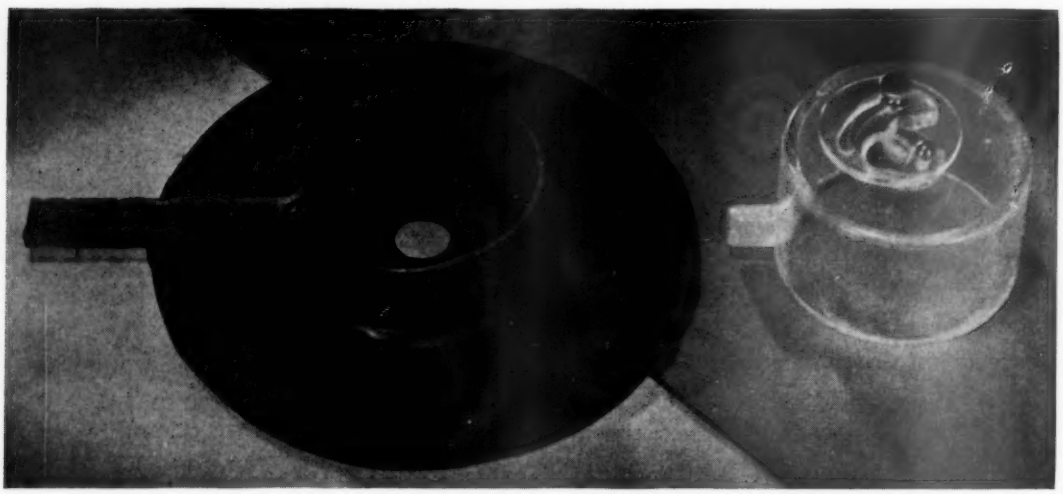

Fig. 1.—Large cup and large rubber base shown separately.

Rubber Base (Fig. 1).—The moulded rubber base, which is made of sterilizable rubber sheeting, has the appearance of a wide-brimmed hat lacking the roof of the crown; it is provided in three sizes to correspond to the cups. The brim, which is the part cemented to the skin, consists of a round sheet of rubber with a small hole in the center; this opening can be easily trimmed to fit the particular ileostomy, etc. To this brim is attached a short cylindrical crown, which fits snugly around the lower half of the cup to prevent leakage. One end of a short rubber tube is attached to the crown above the brim to accommodate the side-arm tube of the cup and to complete the watertight jacket; to the other end of this tube is attached the tubing leading to the waste bottle. If the side-arm tube of the cup is lightly daubed with lubricant, the cup can be easily inserted into (Fig. 2) and enucleated from the rubber base. If, while the apparatus is in operation, it is desired to clean the cup, dilate the ileostomy, or apply a protective paste, all that is necessary is to enucleate the cup from the rubber base, effect the procedure, and replace the cup.

Cement and Cementing.—Firm adhesion of the rubber base to the skin for four to seven days is possible, provided certain precautions are observed: The apposing surfaces of rubber and skin must first be cleansed of oil, water, etc. by naphtha or acetone. With a dry throat stick a uniform layer of cement No.

1 is applied to the skin over the area to be covered by the rubber base; it must be begun at the periphery and continued centripetally in spiral manner to minimize the risk of wetting the cement and imperiling the seal; by pressing the end of a rolled sponge over the stoma during the performance, soilage of the cemented skin can be prevented. A layer of cement No. 2 is then applied to the inferior surface of the rubber brim. The adhesives should be allowed to dry

Fig. 2.—Large cup within the rubber base.

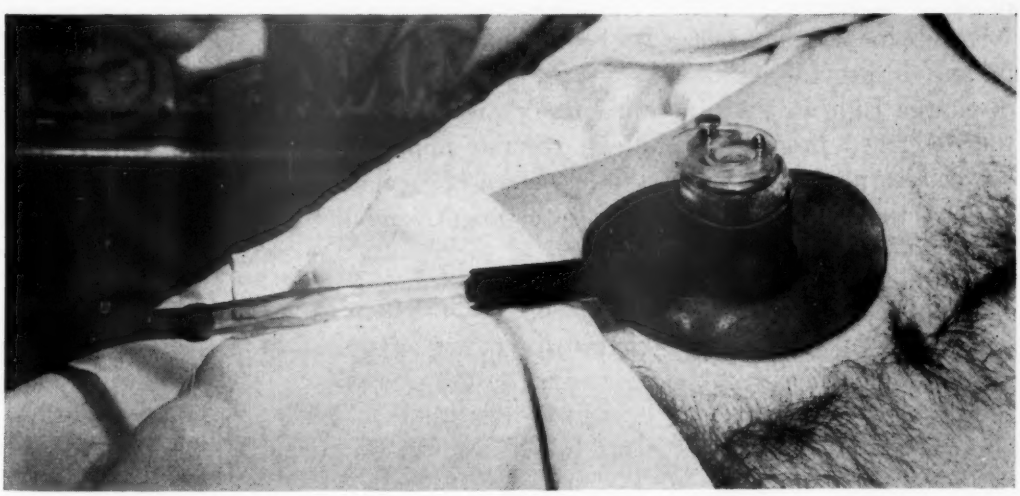

Fig. 3.—Small cup in operation. Rubber tubing attached to the side-arm tube of the rubber base with the aid of a bent glass tube.

for several minutes before the apparatus is gently but firmly pressed onto the skin with the side-arm tube in a dependent position (Fig. 3). If one is dealing with a recently performed ileostomy, aseptic precautions must be observed to prevent infection. The brims, which are large enough to cover freshly sutured wounds and sufficient intact skin for adequate seal, may be trimmed to

the desired size and shape before being cemented. When leakage occurs, the rubber base is slowly and painlessly peeled off the skin with the aid of gauze saturated with naphtha. Before reapplication of the apparatus, the residual cement must be removed from the skin by gentle strokes with the dry finger and/or with gauze impregnated with naphtha. After the rubber base is cleaned with water and dried, the remaining film of cement should be softened by naphtha and loose islands of the adhesive peeled off; meticulous removal of residual cement is tedious and unnecessary. In reapplying the apparatus one repeats the earlier performance.

NURSING CARE

A protective paste,* when applied twice daily in the form of a mound about the ileostomy, serves three important functions: (1) It effectively protects the rim of skin around the stoma from erosion. (2) It shelters the cement from undermining attack by the corrosive ferments and prolongs the rubber-to-skin seal. (3) It shields the projecting ileum from possible wind burn.

Because it is an adsorbent and reportedly inactivates pepsin and trypsin, alumina gel is employed periodically to moisten the stoma and clean the cup. If the gel is excessively viscous it is diluted with water. The neck of an aseptic syringe filled with the suspension is introduced through the intake, and the ileostomy is coated generously every four hours. Most patients are content to effect their own lavage when the purpose and technique are described to them.

To allow limited ambulation, the suction is discontinued, the side-arm tube of the rubber base detached from the tubing leading to the waste bottle, the former clamped, and last a rubber stopper inserted into the intake. Thus the patient is provided with a cup-type, leakproof, ileostomy bag into which the discharge collects. At intervals the patient can empty the cup by reversing the described procedure and can resume ambulation quickly after repeating the earlier performance. If the discharge is especially watery, one may prefer to lead the side-arm tube into a convenient, ambulatory receptacle. A sculletus binder has been found helpful in supporting the apparatus, particularly when the patient is ambulant.

THEORETICAL CONSIDERATIONS

The baffle serves a fivefold purpose by:

1. Admitting atmospheric air in replacement of air exhausted from the cup.
2. Preventing escape of projectile ileal discharge.
3. Allowing periodic irrigation of the stoma and lavage of the cup.
4. Allowing limited ambulation.

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*

1. Aluminum hydroxide gel powder	50 Gm.
2. Kaolin powder	25 Gm.
3. Starch powder	25 Gm.
4. Anhydrous lanolin	125 Gm.
5. Glycerin	50 Gm.
6. White petrolatum	25 Gm.

Mix the ingredients to make a uniform paste.

5. Providing exit for a catheter if indwelling tube drainage of the ileostomy is preferred for the immediate postoperative period. When the catheter loosens, it can be removed by gentle traction and the apparatus set into operation by turning on the suction.

When the apparatus is operating, a steady stream of air enters the cup through the baffle, departs through the side-arm tube, and carries with it any dejecta or irrigating fluid within the cup. Even with a negative pressure up to one and one-half atmospheres in the suction line, the suction in the cup is negligible for practical purposes; however, to avoid wind burn of the projecting ileum, the velocity of the current of air should be kept low by maintaining the effective negative pressure at a level just high enough (three to eight inches of mercury) for prompt removal of the contents.

Though it would seem easy and desirable to effect firm apposition of the apparatus to the skin by means of a constantly maintained, gentle, negative pressure within the cup, this method is not practical for two reasons: (1) Fluctuations in the line of suction result in loss of anchorage of the cup and in leakage. (2) The slight, but inevitable, tenting of the stoma and surrounding skin within the confines of the cup gives rise to edema and discomfort; for this reason one should never occlude the intake opening while the apparatus is in operation.

A plea is made that surgeons carefully choose the site of the ileostomy with reference to the umbilicus and anterosuperior iliac spine; exteriorize the stoma at the inferior angle of the wound; suture the latter carefully with small, plastic sutures or with fine, subcuticular catgut. These precautions greatly influence the immediate and late care of ileostomies and contribute to the comfort and rapid recovery of the patient.

SUMMARY AND CONCLUSIONS

A new and successful apparatus for the care of ileostomies and fistulas is presented.

This simple and durable apparatus is most useful in the early postoperative period following ileostomy, that is, during the phase of profuse discharge of highly irritative, digestive fluids; furthermore, it is efficacious in promoting re-epithelization of eroded and macerated skin around neglected ileostomies (and cecostomies) by virtue of prompt removal of irritative discharges. The apparatus is also successful in the care of fistulas of the small bowel and biliary tract; it should perform well in the care of pancreatic, vesical, and ureteral fistulas.

The tremendous mental and physical lift to the patient and the saving of incalculable time and effort to the nursing staff, not to mention the material economy in laundry and in dressings, are some of the benefits conferred by the use of this apparatus.

For their advice and encouragement, the author wishes to thank Drs. Henry Marble, Leland McKittrick, Chester Jones, Arthur Allen, Claude Welch, Gordon Donaldson, W. Philip Giddings, Daniel Ellis, and Arlie Bock, and Mr. John Murphy. He expresses his appreciation to Hood Rubber Co. Watertown, Mass., for their help in developing the apparatus; also to Dewey and Almy Chemical Co., Cambridge, Mass., for their unstinting help in developing new adhesives. The complete sets and replacements are to be manufactured and distributed by Codman and Shurtleff, Inc., 104 Brookline Ave., Boston, Mass.

STARCH SPONGE—A HEMOSTATIC AGENT

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A NUMBER of highly efficient blood coagulants have recently been introduced into medical practice and have been found of great value. The reasons that have impelled me to describe yet another hemostatic agent is its demonstrated effectiveness and low cost.

In 1947 a patent was granted Drs. Rice and MacMasters of the Northern Regional Research Laboratory of the U. S. Department of Agriculture for the manufacture of an absorbable starch sponge. This sponge was to be used in deep or surface wounds, or for any other requirement of internal use. This patent was assigned to the Government of the United States. The dry sponge is capable of absorbing sixteen times its weight of water, and can absorb appreciable amounts of medicaments such as penicillin, gramacidin, sulfapyridine, etc. The sponge dissolves slowly in the body fluids over a period of several days and the dissolved material is absorbed by the body tissues without harmful results.[1] Absorption is of course preceded by enzymatic action.

It seemed to me that in addition to the absorbent qualities mentioned, the chemical and physical nature of the starch sponge made it highly probable that the sponge also possessed blood coagulating properties.

PREPARATION

Starch sponge may be prepared from any commercial starch.

To begin with, a slurry of starch in water is prepared. This usually contains 5 to 10 per cent of starch by weight. In general, the higher the concentration of starch, the finer the texture of the sponge. At equal concentrations, cornstarch makes a firmer sponge than wheat or potato starch. Additions of medicaments that are to be incorporated into the sponge may be made to the slurry or to the paste.

Sponge formation is brought about by slowly freezing the paste. Freezing must be complete throughout the paste before thawing is permitted.

After thawing is completed, the sponge is squeezed or pressed to remove free water. If the sponge is to be used wet, the material is stored in 70 per cent ethyl alcohol.

The dry sponge is sterilized by cutting it into the desired size and shape, and may conveniently be wrapped in heavy paper and tied with a string. These wrapped pieces may then be placed in a container and autoclaved.

The sponge must immediately be dried and this is accomplished by drying under vacuum in the autoclave, or by subjecting the sponge to a temperature of 95° C. in a drying oven for at least one hour.

The Engineering and Development Division of the Northern Regional Research Laboratory estimated in 1945 that the actual cost of producing the

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sponge exclusive of the cost of the starch, administration, and selling expenses would be 9.48 cents per pound in a plant with a capacity of one ton of starch a day, and 6.67 cents in one with a daily capacity of 5 to 10 tons.

Lee and Lehman[2] in searching for a substance to replace talc which at times is responsible for the appearance of granulomatous growths, found a cornstarch derivative which proved very satisfactory. This starch product replaces talc which is ordinarily used in operating rooms for the preparation of surgeons' rubber gloves. These authors stated, "The fate of this powder (starch) does not offer any great pharmacological problem. Since it is a cornstarch powder, it is simply taken up by the peritoneum and metabolized like any ingested starch."

They quoted MacQuiddy (personal communication) who investigated the sensitizing properties of this substance both in human patients and in animals and failed to demonstrate any sensitizing or anaphylactogenic properties.

Lee and Lehman in experiments with the cornstarch product described in their article showed complete absorption from the peritoneum without any demonstrable inflammatory reaction, and further stated that it produces no adhesions whatsoever.

MacQuiddy and Tollman[3] in an article entitled "An Absorbable Powder to Replace Talc" reported the satisfactory use of a cornstarch derivative treated by physical and chemical means to improve its lubricating value and to prevent gelatinization when autoclaved.

Correll, Prentice, and Wise[4] reported that starch implants in the muscles of rats could not be identified by gross inspection after the tenth day. The stained specimens revealed fragments of starch through the fiftieth day. No significant tissue reaction to this material was observed, but the forty- and fifty-day specimens revealed an extraordinary cellular infiltration, largely of mononuclear phagocytes. The type of phagocyte that usually engulfs lipoids seems to be attracted by this material invading and replacing it.

Although our problem was more concerned with hemostasis than with adhesions, nevertheless we performed experiments to determine the action of starch in the presence of hemorrhage and its effect on the peritoneum. The employment of even a markedly efficient hemostatic agent that produces crippling adhesions would indeed only be justified in the direst emergency. Fortunately this did not prove to be the case when starch sponge was used.

We found the sponge to be an excellent hemostatic agent in the rabbit. Experimental animals survived in whom we incised either the large veins of the ear, the femoral vein, or the inferior vena cava. In the case of the auricular or femoral veins the fellow of the opposite side was used as a control. The vena cava experiments were controlled by administering no treatment to some of the control animals, and treating others with pressure and gauze packing.

All the untreated animals, as expected, died within one to two minutes after the vena cava was incised.

When plain gauze was pressed against the opening in the vena cava and left in situ as a pressure pack, hemostasis resulted. When these animals were autopsied approximately one month after operation, the adhesions encountered

were so dense, and the intestines so compromised, that at present with the ready availability of efficient hemostatic agents the practice of employing plain gauze as a packing in cases of hemorrhage should be abolished, except in those instances where no other suitable hemostatic substance can be obtained. Another drawback to the gauze pack is its tendency to disturb the clot and tear tissues on removal so that bleeding commences again.

In every case where the starch was properly applied to any of the venous structures mentioned previously, including the vena cava, the animal survived.

We found that the best method of obtaining hemostasis with the starch sponge was to moisten one end of the dry starch bar with sterile water or saline solution, and to cover the opening in the vein with this moistened end simultaneously creating pressure by bearing down on the dry end of the bar. When all bleeding ceased, usually a matter of one to two minutes, the whole or part of the bar was left in situ.

Large pieces of starch were left in the peritoneal cavity of some animals so that the effect of massive pieces on starch sponge could be studied.

Taking into consideration the fact that the vena cava is located in the retroperitoneal space, the cellular tissue of which is almost embryonal in its reaction to stimuli such as irritants, foreign bodies, etc., the adhesions we found at autopsy, usually performed three to four weeks after operation, were surprisingly moderate.

To study the reaction of the general peritoneal cavity to the sponge rather than that in the retroperitoneal space we introduced large pieces of dry and wet sponge among the intestinal coils without opening any large vessel. At autopsy gross inspection in the majority of these animals revealed none or minimal adhesions. One animal, however, showed a walled-off sac attached to one of the intestinal coils. Another animal showed a small granulomatous lesion in the lower angle of the peritoneal incision. It should be taken into account that much more starch was used in these animals than would ever be found necessary to employ in a human being weighing many times more than the experimental animal. All of these animals survived, appeared healthy, and had gained in weight in the three- to five-week interval between operation and autopsy.

Frantz[5] in discussing Oxycel stated that cysts are sometimes found in serous cavities where a relatively large mass of material is surrounded by serous membranes. Such cysts usually resorb.

CLINICAL CASES AND SUMMARY

We have to date used the starch sponge in fifty-three gynecologic and obstetric patients to control bleeding. In addition, the Mohels (ritual circumcisers) have used the cornstarch powder as prepared by the United States Department of Agriculture in approximately one hundred cases.

Intraperitoneal applications were made in twenty patients; in the course of operations such as hysterectomy, myomectomy, and in one case of a ruptured corpus luteum cyst of pregnancy. It was employed in nine cases of cesarean section; in seven of these patients it was used to control bleeding on the uterine

surface, and in two patients the sponge was introduced into the uterine cavity, via the uterine incision.

In a patient who had several hemorrhages due to retained secundines following full-term pregnancy, several pieces of starch were introduced into the uterine cavity. This was done only after profuse bleeding continued despite the fact that the curette failed to locate any additional products of conception. Immediately after the introduction of the starch, bleeding ceased and no cervical or vaginal packing was employed.

An intrauterine application of gauze bandage impregnated with starch sponge was performed on the second post-partum day of a patient who suffered a severe post-partum hemorrhage despite the fact that the uterus and vagina were tightly packed with gauze. This patient had a splenectomy at the age of 12 years because of thrombocytopenic pupura. On the basis of this history the obstetrician had taken the precaution of giving her transfusions before and after delivery and tightly packing the uterus with plain gauze. Despite these precautionary measures a severe hemorrhage ensued and she exhibited many of the signs and symptoms of impending death. The gauze pack was removed and a starch sponge pack introduced. The bleeding ceased almost immediately, and she was discharged from the hospital in good condition on the eleventh post-partum day.

We were fortunate in having another patient present herself in whom a control observation was possible. This case concerns a woman of 70 years. She had a prolapse of the uterus, and had worn a pessary for many years. Her doctor removed the pessary because of pressure symptoms and after several weeks an attempt was made to reinsert it. Great difficulty was encountered and the attempt at reinsertion was abandoned. However, the vaginal walls had sustained multiple lacerations, and hemorrhage ensued. Several vaginal packings of plain gauze were ineffectual in controlling the bleeding. She was admitted to the hospital where the gauze pack was removed and starch sponges substituted. The sponges were maintained in position by placing a small amount of gauze in the vaginal orifice external to the outermost starch sponge bar. The bleeding was promptly controlled.

Starch sponge in powder form, or gauze impregnated with the starch sponge powder, was used eleven times after cervical cauterization, eighteen times in the course of vaginal plastic operations, twice in the rectum after removal of polypi and cauterization of hemorrhoids, and once in the thigh after the resection of fascia lata for purposes of transplantation.

The Mohels stated that they have used it with satisfaction in approximately one hundred ritual circumcisions.

There was no mortality in this series. There was one morbidity that might have possibly been due to the intrauterine introduction of starch sponge. This occurred in a patient who had retained secundines and continued to bleed after curettage. The uterus was packed with starch sponge. A few hours after operation her temperature rose to 105° F. One cannot be certain that the starch sponge was the responsible agent, for she received a blood infusion and the possibility of intrauterine infection could not be excluded. Both of the latter factors

are competent producing causes for the reaction that this patient exhibited, and either might just as well have been the etiologic mechanism. The patient left the hospital in good condition on the fourth postoperative day.

CONCLUSION

Starch sponge is an efficient hemostatic agent. Its effects appear to be purely local and its hemostatic action is probably due to its gel formation. It can absorb many times its weight in blood. This causes the sponge to swell and to exert pressure, thus forming a mechanical obstruction to the flow of blood.

Acknowledgment.—The author wishes to thank Dr. M. M. MacMasters of the United States Department of Agriculture and her staff for their fine cooperation, Dr. B. Lapan for his invaluable assistance, Drs. A. A. Angrist, J. C. Ehrlich, H. Wallerstein, and A. Schwarz for examination of tissue and valuable suggestions, and Miss Beatrice Ferrill, R.N., for ingeniously preparing starch sponge bandage.

ADDENDUM

Since this article was submitted, starch either in the form of the sponge, the powder, or the impregnated gauze bandage has been used in forty-one additional patients.

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Case Reports

PRIMARY SPLENIC SARCOMA

Report of Case

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PRIMARY malignancies of the spleen are rare. Hausmann and Gaarde collected 178 cases in 1940, nine of which they added from the Mayo Clinic. Mentzner and Jones added two cases from the Cleveland Clinic in January, 1948, ten cases having appeared in the meantime, bringing the total to 190. These two cases constituted the only primary malignant tumors seen in that clinic in two decades, and the one operative case was the only splenectomy for primary splenic malignant disease among 20,000 major surgical procedures.

CASE REPORT

A 62-year-old mother of three children complained for three months of pain in the left side of the body including arm, shoulder, chest, and upper abdomen. On self medication with vitamins, the arm and shoulder pain became better, but the abdominal pain became worse. Flatulence and occasional vomiting occurred, and she noted that deep inspiration and eating accentuated the pain in the left upper abdomen. She had lost twenty-seven pounds in weight, the appetite became poor, there were no bowel changes, and the vomitus never contained blood. She had had bronchial asthma for thirty-seven years, starting with what she guessed was tuberculosis. There had been no attacks for years until two weeks before admission to the hospital on Dec. 10, 1947.

Examination revealed a somewhat obese woman of short stature. There were râles at the left base, the left diaphragm was elevated about two inches, and a firm, moderately fixed mass was palpable in the splenic area. It extended about 2 to 3 cm. below the costal margin and was about 4 to 5 cm. wide. There was only one palpable lymph node, deep in the left axilla.

A tentative diagnosis of malignancy involving the left diaphragm was made at the first visit, and she was referred for x-ray study. The chest revealed several healed tuberculous lesions. The barium enema was negative. The stomach was reported to show a lesion at the fundus but the roentgenologist suggested a gastroscopy, since his findings were somewhat equivocal. The gastroscopy disclosed no lesion of the stomach, but since the area of the supposed tumor lay where the gastroscope could not surely reveal it, another gastric x-ray was recommended. This more definitely suggested a gastric lesion. The gastric analysis was normal. Another roentgenologist decided the lesion was extragastric. Intravenous pyelograms revealed normal kidneys. In view of the palpable mass in the splenic area, lack of hematemesis, normal gastric analysis, and the other findings enumerated, a diagnosis of malignant tumor of the spleen was agreed upon.

On entrance to the hospital, the patient had a temperature of 102° F. and many râles in the chest. The red cells in the blood varied from 3.67 to 5.96 million per cubic millimeter during the preoperative period. The leucocytes ranged from 11,800 to 17,850 per cubic millimeter of blood, and the differential smear ranged between 78 and 91 per cent neutrophiles, 9 and 12 per cent lymphocytes, 1 and 5 per cent monocytes, and an occasional undifferentiated "blast" cell. A definite shift to the left developed preoperatively with the presence of 14 per cent juvenile forms being observed at one time. A lymphoma as the source of the occa-

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Fig. 2.

Fig. 1.

Fig. 1.—Sectioned spleen presenting capsular surface. The left half presents the hilum, and the right half is largely the diaphragmatic surface.

Fig. 2.—Cut surface revealing large reticulum cell lymphosarcoma.

sional "blast" cell visualized in the peripheral blood was considered as probable on clinical correlation. The patient felt worse, and dated the increased malaise from the time of the gastroscopy. The operation was postponed from day to day until two weeks had elapsed. During this period, three chest x-ray pictures showed no change in the original findings, and in spite of intensive treatment the fever was not reduced.

Under intratracheal anesthesia, the patient was placed upon the right side in preparation for the combined abdominothoracic incision as described by Garlock. The abdomen was opened by a high incision lateral to the rectus muscle. The stomach was free of disease, there were no palpable metastases, and the spleen was enlarged and densely adherent to the diaphragm. It was felt that abscess of the spleen could not be ruled out, and it was decided to remove the spleen. The incision was extended across the costal margin and through the

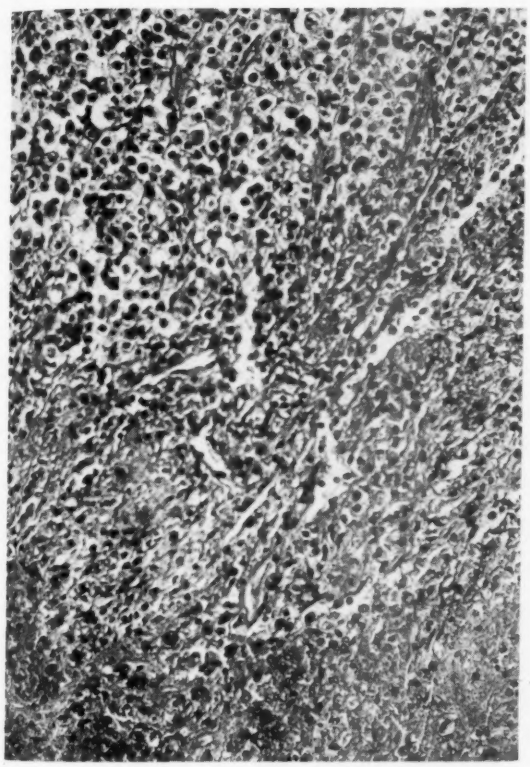

Fig. 3.

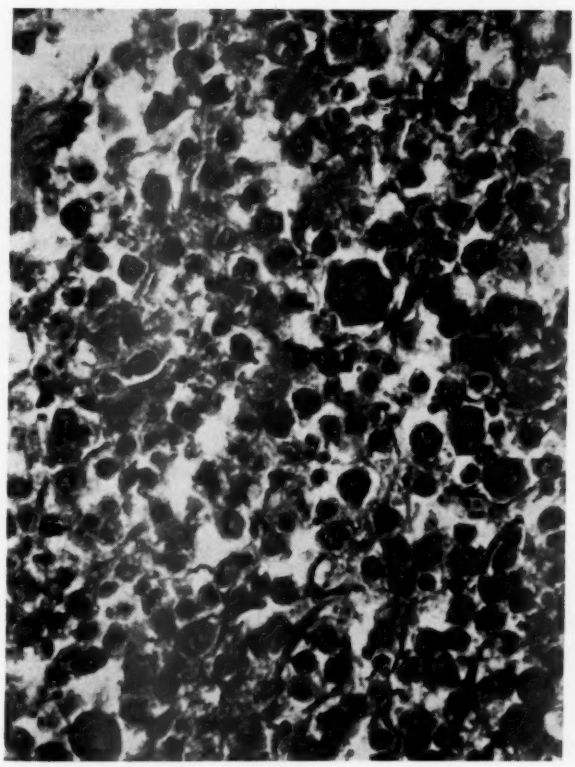

Fig. 4.

Fig. 3.—Undifferentiated large reticulum cell bordering on an area of necrosis (hematoxylin and eosin stain).

Fig. 4.—Reed-Sternberg type of giant cells surrounded by the more characteristic undifferentiated reticulum cells (hematoxylin and eosin stain).

eighth interspace posteriorly. The lung was adherent to the diaphragm and was freed easily. The diaphragm was replaced by grayish tissue and a portion was removed from the superior surface for frozen section. It revealed anaplastic malignant tissue. Resection of the left half of the diaphragm and replacement by ox fascia were discussed and rejected. The spleen was separated from the diaphragm and removed. The phrenic nerve was crushed, and the wound closed with chromic catgut encircling the ribs and black silk elsewhere, with no drain.

Recovery was largely uneventful, although the fever persisted. The wound healed without incident. Fluid to the amount of 850 c.c. was removed from the left side of the chest two weeks after operation, and showed no leucocytes or organisms on smear, and no growth on culture. X-ray treatment was started one week after operation but was not tolerated well and was given up. The patient left the hospital sixteen days after operation and died at home 16 days later. An autopsy was not done.

The spleen was enlarged, weighed 870 Gm., and measured 16 by 13 by 12 cm. Approximately three-fourths of the spleen was replaced by a 12 cm. in diameter, spherical, white, relatively firm tumor which presented prominent roughened adhesions on its diaphragmatic surface. The usual reddish rubbery type of spleen was present as a rim on two sides. The hilum included a portion of the pancreas which was grossly recognized and this measured 1.5 to 2 cm. in diameter. The fatty fibroconnective tissue attached to the hilar vessels included detectable lymph glands ranging between 5 and 15 mm. in diameter. One of these appeared to be subtotally replaced by a yellowish-brown tumor while three of the larger lymph glands presented a light pink, meaty, cut surface. Sections of spleen revealed a semicartilaginous type of tumor whose central portion was light yellow and of a soft putty nature. Tumor was not clearly demarcated and the detectable spleen peripherally presented redder, softer, irregular, poorly defined points of invasion.

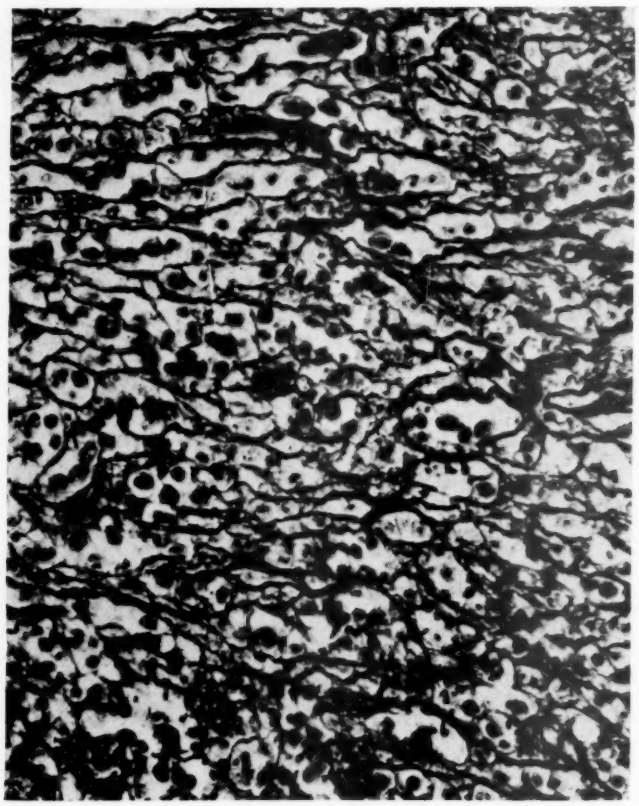

Fig. 5.—Wilder's reticulum stain showing abundant reticulum.

Microscopic examination revealed the greater portion of the tumor tissue to be necrotic. Tumor cells were undifferentiated, relatively large (two to three times the size of a lymphocyte), and revealed no definite architectural pattern but an unorganized diffuse arrangement in broad sheets. Tumor cells presented large hyperchromatic nuclei, prominent enlarged nucleoli, many mitoses, and an abundant, misty type of cytoplasm. Tumor cells, for the most part, were observed as relatively uniform but in localized areas there were prominent multinucleated giant cells which, at times, presented horseshoe-shaped hyperchromatic nuclei and light eosinophilic cytoplasm. Wilder's reticulum stain revealed prominent interwoven reticulum throughout the greater portion of the tumor.

Sections of the pancreas, fatty fibroconnective tissue of the hilum, and a portion of the diaphragm revealed direct extension of the described tumor. One lymph gland was found to be subtotally replaced with tumor, essentially similar to that of the spleen, while three lymph

glands revealed a nonspecific hyperplasia with no tumor involvement. This lesion histologically was classified as reticulum-cell lymphosarcoma on the basis of the large and uniform undifferentiated cells and the abundant reticulum demonstrated by Wilder's reticulum stain. The large multinucleated giant cells which at times resembled Reed-Sternberg cells, suggested Hodgkin's sarcoma as a possible diagnosis. Clinicopathologic correlation indicated this tumor as a primary lesion of the spleen.

COMMENT

It seems probable that this disease produces few if any symptoms until neighboring structures are involved, whereupon the prognosis becomes almost hopeless. After a growth of this sort involves adjacent structures, removal merely hastens the end. If it can be attacked before such direct extension has occurred, the prognosis seems to be remarkably good. The combined abdominothoracic incision is excellent, permits exploration before the chest is opened, and should have a wide range of usefulness. Whether a rib is removed or the intercostal incision is used would seem to depend on the prejudices of the operator.

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Surgical Technique

THYMECTOMY FOR MYASTHENIA GRAVIS

SURGICAL TECHNIQUE

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ROCHESTER, MINN.

ALTHOUGH little is known about the thymus gland and its functions, a considerable body of evidence has accumulated to indicate that there is a definite relationship between this gland and the disease, myasthenia gravis. The first surgical attempts to treat patients with myasthenia gravis by removal of the thymus gland were made by Sauerbruch.[1] These attempts were made before neostigmine had been developed for the medical treatment of the disease and before thoracic surgery had advanced to its present status.

Blalock and associates[2] were the first to perform thymectomy for myasthenia gravis with apparent success. Since their report, a considerable number of thymectomies have been reported. There has been some variation in the results obtained from operation but most surgeons have agreed that thymectomy does not provide a surgical cure of myasthenia gravis in all cases. Some patients have apparently benefited greatly, but in others the disease has apparently not been affected. It has been impossible, from experience thus far, to determine which patients with myasthenia will benefit from operation and which will be unaffected. It has, likewise, been impossible to establish any relationship between the pathologic changes found in the thymus gland at operation and the severity of the myasthenia gravis, or to predict, on the basis of observed pathologic features, the benefit that might be expected from operation. Although we cannot predict the benefit to be gained by thymectomy in the treatment of myasthenia gravis in any individual case, some patients have shown improvement in the severity of myasthenia after thymectomy, and in a few cases complete remission of the disease has occurred. In no case has myasthenia gravis become worse after operation.

It has been our policy to suggest thymectomy in the treatment of patients with moderately severe myasthenia gravis and patients whose disease appears to be progressive. We have not urged operation in cases of mild myasthenia gravis which is well controlled by neostigmine therapy, and we feel strongly that operation should be delayed in patients with very severe manifestations of the disease until it is in remission, since the severely myasthenic patient is a very poor surgical risk.

PREOPERATIVE CARE

Preoperative preparation is extremely important. The patient should be in the hospital for a few days before operation if possible. This permits complete rest and a period of observation so that the requirements of the patient

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for neostigmine can be determined accurately. Myasthenic patients are very susceptible to respiratory infections and should be fully protected from exposure. A preoperative course of penicillin may be indicated. Most female patients with myasthenia gravis note an exacerbation of the disease just before the menstrual period. Operation should be deferred until menstruation has ceased in these patients.

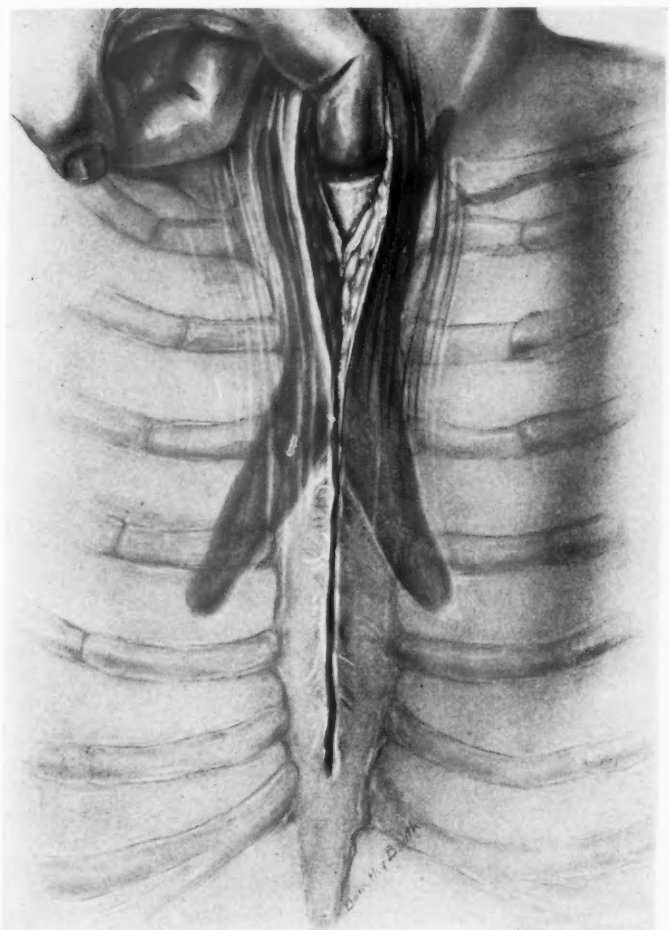

Fig. 1.—The incision extends from the manubrial notch to the xiphoid process. The soft tissues are pushed away from the posterior wall of the sternum and the sternal chisel is inserted.

Many myasthenic patients are thin, weak, and undernourished because of their difficulty in chewing and swallowing. Every effort, even including feeding by tube, should be made during the preoperative period to restore the patient's nutritional status. Oral neostigmine therapy as required by the individual patient should be continued up to the time of operation. Heavy preoperative sedation is to be avoided. We prefer to avoid the use of barbiturates for preoperative sedation since myasthenic patients are depressed excessively by such drugs. Just before operation the patient should be given 1.0 to 1.5 mg. of neostigmine methylsulfate, 1/8 to 1/6 gr. (0.008 to 0.01 Gm.) of morphine, and

1/150 gr. (0.00043 Gm.) of atropine subcutaneously. The anesthetic of choice is nitrous oxide, oxygen, and ether administered through an intratracheal tube. Sodium pentothal and curare are definitely to be avoided.

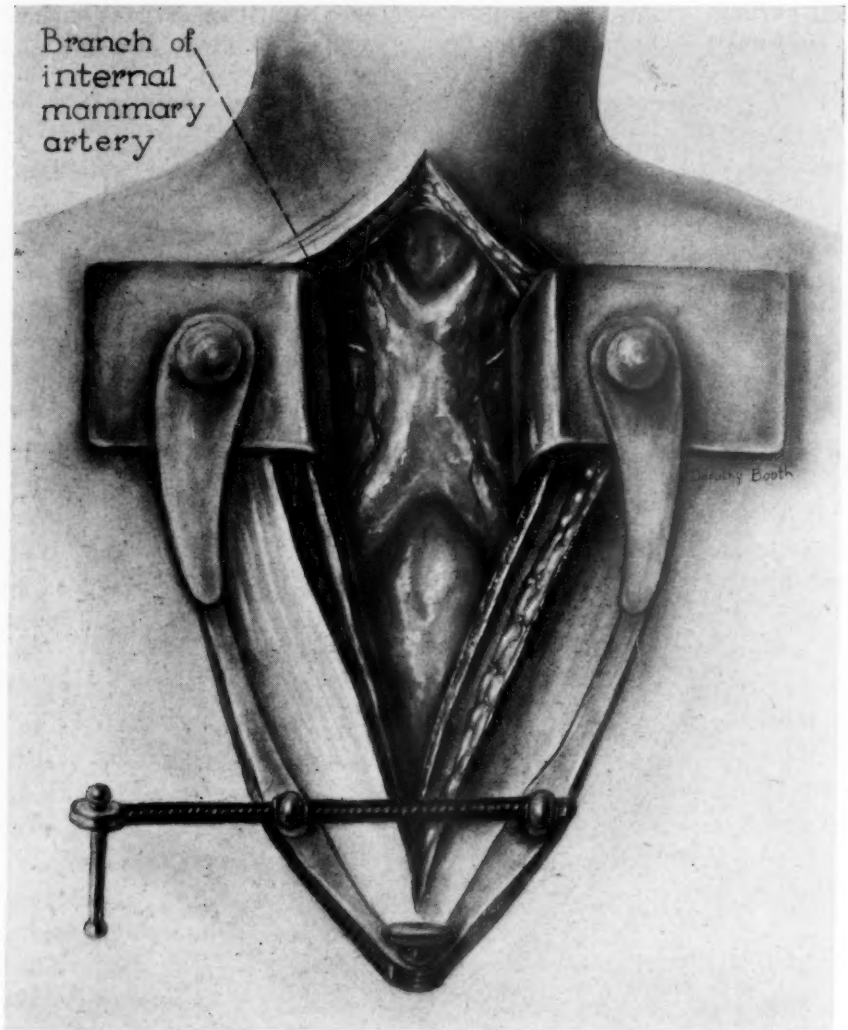

Fig. 2.—The split sternum is separated, exposing the thymus.

OPERATIVE TECHNIQUE

A variety of surgical approaches has been used in operations upon the thymus gland. Partial thymectomy has been performed from a cervical incision. Since the thymus gland extends well down over the pericardium, this approach does not permit resection of more than a small portion of the thymus and is entirely inadequate. In the case of large thymic tumors which occur not infrequently in instances of myasthenia gravis, it may not be possible to obtain adequate exposure through a sternum-splitting incision, and in such cases a posterolateral transpleural approach to the anterior mediastinum may

be necessary. In some cases this approach will not permit complete removal of the portion of the thymus gland which extends up into the neck in the region of the inferior poles of the thyroid gland.

The most satisfactory approach for complete removal of the thymus gland in patients with myasthenia gravis is the sternum-splitting incision. The skin is incised vertically over the sternum from the manubrial notch to the xiphoid process. The dense layer of pretracheal fascia attached to the posterosuperior edge of the manubrium is cut and a finger is inserted behind the manubrium,

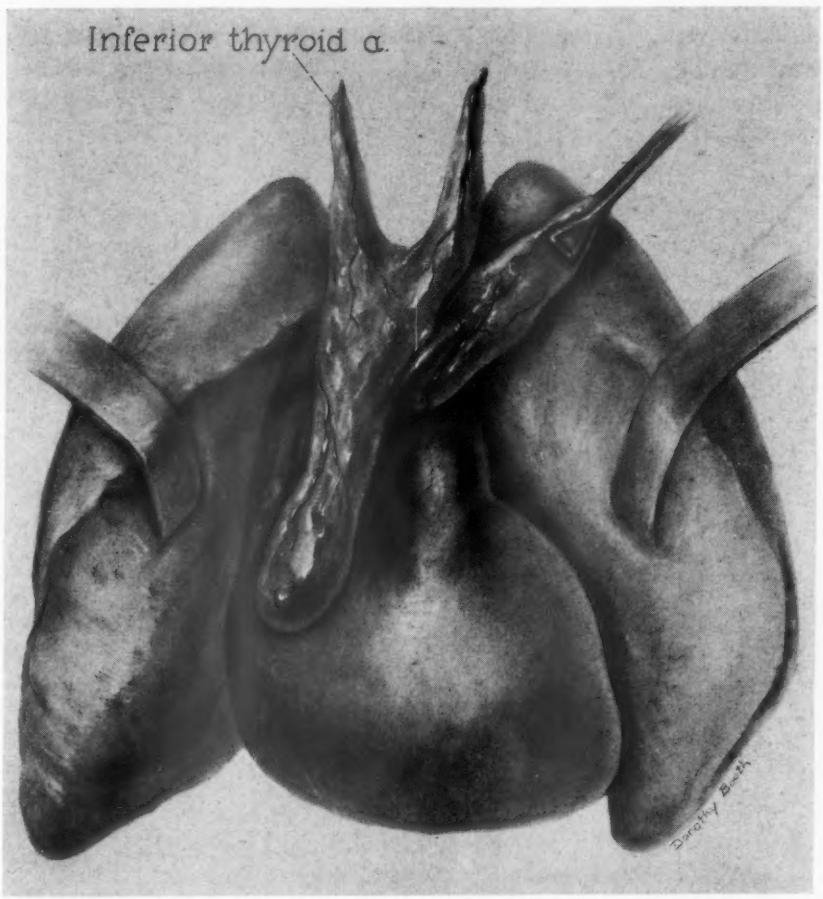

Fig. 3.—The lower lobes of the thymus gland extend down to the pericardium, the upper lobes up into the neck.

pushing the soft tissues away from the base (Fig. 1). A Lebsche sternal chisel is then inserted and the manubrium and sternum are split in the midline to the xiphoid process. The manubrium is a rather dense bony structure, particularly in adults, but the sternum splits quite easily. There may be considerable oozing of blood from the sternal marrow. A self-retaining retractor is inserted and the split sternum is spread apart exposing the anterior mediastinum (Fig. 2).

At first glance the thymus gland may not be noted in the loose areolar and fatty tissue of the anterior mediastinum, but a little dissection will disclose it. It is pinkish gray in color, has a fine granular-appearing surface, and has a

very thin but definite capsule in most instances. It is a bilobed gland joined in the center just over the left innominate vein, with thin extensions going up toward the lower poles of the thyroid in the lower cervical region and rather broad, flat lower lobes spread out over the pericardium. The gland receives its blood supply from the branches of the inferior thyroid artery which go to the upper poles, and from branches of the internal mammary artery which enter the gland laterally at about the level of the isthmus that joins the two sides. The venous drainage from the gland is through one or occasionally two vessels passing directly from the posterior wall of the isthmus of the gland into the left innominate vein. These blood vessels are remarkably constant in their location and number.

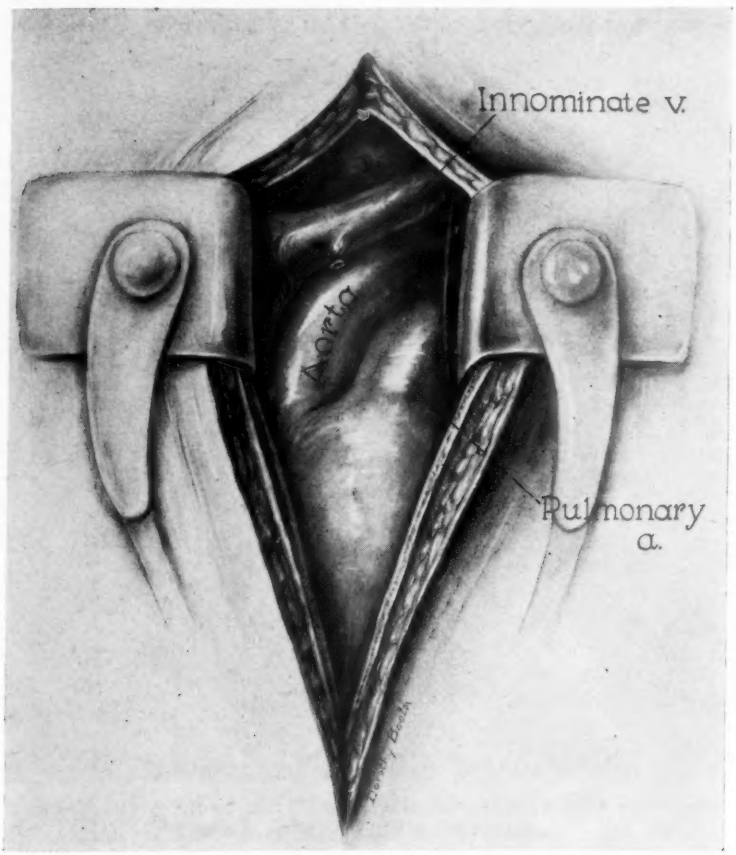

Fig. 4.—After removal of the thymus gland, the great vessels in the superior mediastinum are exposed.

The thymus gland is likely to be quite adherent to the pleura laterally and it is very easy to open the pleura inadvertently during the dissection. The gland extends posteriorly to the level of the phrenic nerves and extends down over the pericardium. Since the gland is quite friable it must be handled gently (Fig. 3). After the gland has been completely excised, the arch of the aorta and its branches, the pulmonary artery, the left innominate vein, and the anterior pericardium are completely exposed (Fig. 4).

We formerly used encircling steel wire sutures around the sternum for its approximation in closure. There was always some danger of injuring the internal mammary artery as these sutures were inserted and we now use only interrupted catgut or silk sutures in the fascia and periosteum on the anterior surface of the sternum (Fig. 5). The subcutaneous tissues and skin are approximated with interrupted sutures. No drains are used. If the pleura has been opened inadvertently during the operation no attempt to close the opening is made but all air is aspirated from the pleural space by means of a catheter, and the anesthetist maintains expansion of the lung with positive pressure as the wound is closed.

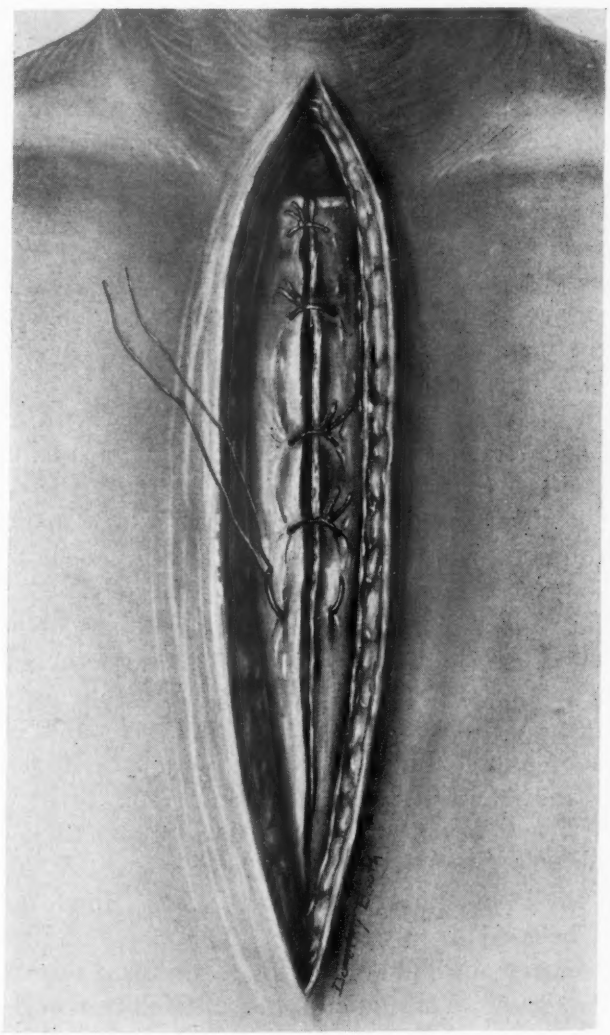

Fig. 5.—Sternum is approximated with interrupted stitches in the anterior fascia.

It should be mentioned that although the thymus gland usually lies anterior to the innominate vein, in two cases in our experience the gland lay entirely behind the vein and in another the right lobe lay anterior to the vein and the left lobe posterior to the vein.

Occasionally during thymectomy performed on patients with myasthenia gravis, some weakness of respiratory effort may be noted. Neostigmine methylsulfate in 1.0 mg. doses should be available in the operating room and a dose should be administered subcutaneously at once under these circumstances. Neostigmine causes some increase in oral and tracheobronchial secretions. The pharynx and tracheobronchial trees should be aspirated as necessary during the operative procedure and particularly at the end of the operation. Occasionally postoperative bronchoscopy will be necessary to remove retained secretions.

POSTOPERATIVE CARE

Postoperatively the patient should be placed in an oxygen tent for twelve to twenty-four hours in most instances. An aspirating device should be readily available to remove secretions from the mouth and pharynx until the patient has recovered from anesthesia. A Drinker-type respirator should be kept in readiness, preferably in the patient's room, and the patient should be placed in the respirator if there is any evidence of weak or inadequate respiratory function in spite of neostigmine therapy. A respirator has been lifesaving in several of our cases. Neostigmine methylsulfate, in 1.0 mg. doses, should be given subcutaneously every two to three hours postoperatively, and this dose may be doubled or given every hour if the patient's condition is not satisfactory. Theoretically it may be possible to give a patient too much neostigmine. From a practical standpoint it is much better to err on the side of giving more neostigmine than is necessary to the postoperative patient with myasthenia gravis than it is to err on the side of giving too little. Oral administration of neostigmine bromide, in doses of 15 mg., should not be resumed postoperatively until the patient is able to swallow and then the dosage should be adjusted to the patient's requirements, which are usually met by about the same program that the patient had found to be adequate preoperatively.

A sudden and dramatic relief of the manifestations of myasthenia gravis is not to be expected. Some of our best results have occurred in patients who were not able to reduce their neostigmine requirements for several weeks or months after operation. Increased salivation and abdominal cramping incident to the large doses of neostigmine required in some patients postoperatively can be minimized by the administration of atropine sulfate in doses of $\frac{1}{150}$ gr. (0.00043 Gm.). Heavy postoperative sedation of any kind is to be avoided except in patients who become so nervous and exhausted that it is necessary to place them in the Drinker respirator for a time. Small doses of codeine or morphine should be used to control pain. Large quantities of pain-relieving drugs are not necessary since patients with this disease seem to have relatively little postoperative pain. The patients are allowed out of bed in forty-eight hours and are usually dismissed from the hospital within one week.

RESULTS OF OPERATION IN EIGHTY-FIVE CASES

Our experience with operations on the thymus gland in patients with myasthenia gravis is based on eighty-five cases. Thirty-one of the patients had tumors of the thymus; fifty-four did not have tumors. The presence of a thymic

tumor had been demonstrated by radiologic examination preoperatively in thirty instances. In only one instance was a tumor of the thymus suggested by radiologic examination and not found on surgical exploration. The high incidence of thymic tumors in this group of cases does not represent the true incidence of thymic tumors in myasthenia gravis; the true incidence is about 15 per cent. This high figure results from our policy of urging all patients with thymic tumors to have an operation regardless of the status of the myasthenia gravis because of the potential danger of the tumor.

Thymectomy was often offered to patients without evidence of thymic tumor if the myasthenia gravis was moderately severe or progressive, but was never urged under any circumstances. Our rather conservative surgical attitude is indicated by the fact that in a period of seven and one-half years, 75 patients were operated upon while 142 other patients with myasthenia gravis observed in the same period were not operated upon.

In our series of eighty-five operations on patients with myasthenia gravis, there were seven deaths. Five deaths occurred in patients with tumors, and two in those without thymic tumors. The deaths, with one exception, were due to complications of myasthenia gravis rather than related to the operative procedure itself. There were no wound complications. Unless complications related to the myasthenia gravis developed, patients were able to leave the hospital within one week or ten days after operation in all cases.

Myasthenia gravis is a disease that varies greatly in severity and is subject to remission and exacerbation without apparent cause. This fact has made an accurate evaluation of the effect of thymectomy on the course of the disease very difficult. However, we have attempted to make a careful follow-up study of 217 patients with myasthenia gravis by comparing a group of 75 patients treated by thymectomy with a group of 142 patients treated by medical measures, observed over the same period of time. It had been our clinical impression that the patients who had thymectomy had shown some improvement over those not operated upon. However, our follow-up study has failed to demonstrate any significant benefit from thymectomy that can be attributed to the operation. Over the period of observation, ranging from one to seven and one-half years, the course of the disease was essentially the same in the patients who did not undergo operation as in those who did. While it must be admitted that thymectomy apparently does not benefit the myasthenic patient, it should also be noted that there was no instance in which the symptoms of myasthenia gravis could be said to have been made worse.

CONCLUSIONS

As a result of our experience, we have come to the following conclusions regarding the thymus gland and myasthenia gravis:

1. There is some connection between the thymus gland and myasthenia gravis. It cannot be pure coincidence that tumors of the thymus occur in 15 per cent of all cases of myasthenia gravis. The exact nature of the relationship between the thymus and myasthenia gravis is unknown.

2. All patients with myasthenia gravis should be studied thoroughly for evidence of thymic tumors. Simple posteroanterior roentgenograms do not give an adequate basis for diagnosis since the tumor is often hidden behind the sternum. Roentgenoscopic examination as well as lateral and oblique films will be necessary to demonstrate many thymic tumors.

3. Thymectomy should be advised in all instances of thymic tumor unless the condition of the patient makes the risk of operation prohibitive. Such a tumor may be well encapsulated and apparently benign. In other instances the tumor may show malignant characteristics with invasion of surrounding tissues. In a few instances the tumor has proved to be inoperable due to invasion of the pleura and lung, pericardium, and great vessels.

4. Thymectomy may be suggested in carefully selected cases of myasthenia gravis if the disease is moderately severe or progressive. It should not be advised if the disease is very mild or very severe because the patient with mild disease will probably not be benefited and the patient with very severe disease is a very poor surgical risk. The results of thymectomy in the treatment of myasthenia gravis are unpredictable. We have not been able to show statistically that patients with myasthenia who had had thymectomy have benefited materially from operation when compared with a group treated by medical means.

REFERENCES

1. Sauerbruch: Quoted by Blalock, Mason, Morgan, and Riven.[2]
2. Blalock, Alfred, Mason, M. F., Morgan, H. J., and Riven, S. S.: Myasthenia Gravis and Tumors of the Thymic Region, Ann. Surg. **110:** 544-560, 1939.

Editorial

Further Specialization

WITHIN the past several months two major conferences have been held to discuss a specific pathologic process: one, in New York, the First Annual Scientific Meeting of the Gerontological Society and the other in Memphis, the National Cancer Conference. Those who attended both meetings may have been struck by the similarity of approach at these meetings. Because the study of both the aging process and cancer concerns many diverse groups, there were present biologists, internists, surgeons, the medical and surgical specialists, as well as the social scientists to contribute to the discussions.

In spite of the fact that we now have the oncologist and may soon have the gerontologist, it must be apparent that significant advances in the knowledge of both malignant disease and the aging process will require the cooperation of many disciplines. There is a grave danger in further multiplying the medical and surgical specialties without giving sound thought to what may be sacrificed for that which is gained.

One is reminded of Harvey Cushing's statement on this subject: "The specialties are justified solely by their productiveness. It might be wise for each of them occasionally to come back to the mother tree for suckling."

It is seriously questioned whether oncology or gerontology should be treated as specialties to be organized as isolated subjects in medical teaching or in residency training except at a graduate level above the "mother tree." Specialization in these fields should originate from the parent specialty, but specialty boards in either field are unnecessary.

Medical education must be sufficiently broad to train internists with a special interest in the medical problems of old age, as well as surgeons with a special interest in the surgical problems of old age. The same is true for oncology. In each instance the special interest from the standpoint of clinical practice should be engrafted on thorough training in internal medicine or general surgery.

—I. S. Ravdin.

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

MALIGNANT NEOPLASMS OF THE THYROID

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IT IS well known that in a considerable proportion of cancers the ultimate malignant state is an attribute acquired only after a variable interval of time in a well-recognized progression from a benign precursor. In attempting to reduce the number of deaths from cancer of any organ, a most important consideration is the early recognition and eradication of precancerous lesions where such are known to exist.

Many authors have recently stressed the high incidence of malignancy in adenomatous goiter. Indeed, so frequent is the relationship of thyroid adenoma to malignancy that the attitude of regarding all adenomatous thyroid glands as having significant malignant potentialities is constantly gaining adherents. Data from the University of Michigan Hospital support this attitude, and the corollary that (unless strong contraindications exist) thyroidectomy should be recommended whenever the diagnosis of adenomatous goiter is made, regardless of the presence or absence of hyperthyroidism.

This report makes available the material from the departments of pathology and surgery, together with a selective review of the literature pertaining to thyroid malignancy.

INCIDENCE

During the ten-year period from June, 1935, through July, 1945, thyroidectomy was performed upon 1,326 patients in this hospital. Cancer was found in 61 instances, or an incidence of 4.6 per cent among all surgically treated goiters. In the series recently reported by Horn and associates,[31] the incidence was 3.0 per cent of all surgically treated goiters (62 carcinomas in 2,079 surgical goiters). Ward[58] also reported an incidence of 3.0 per cent (168 cases of malignancy in 5,439 surgical goiters). Foss[24] averaged the reports of 11 authors and obtained a figure of 2.37 per cent as the incidence of malignancy in surgically treated goiters.

In the present series it was felt worth while to study the cases in a manner that would correlate the possibility of malignancy to the type of goiter found on physical examination. Accordingly, three groups were selected: the first consisting of patients having a palpable nodular or adenomatous goiter on physical examination (and this group was further subdivided into those having multiple nodules and those having a single nodule); the second group consisting of patients having a palpable diffuse goiter without clinically discernible nodules; and the third group being comprised of patients presenting no palpable thyroid enlargement. Table I summarizes these data.

TABLE I. CLINICAL GROUPING BASED ON TYPE OF GOITER PRESENT

	TOTAL NUMBER OF CASES		TOTAL NUMBER MALIGNMENT		PER CENT MALIGNANT	
	FEMALES	MALES	FEMALES	MALES	FEMALES	MALES
Group I. Palpable nodular goiter	693	143	45	13	6.5	9.1
(a) Multinodular	562	115	34	11	6.0	9.56
(b) Single nodule	131	28	11	2	8.4	7.14
Group II. Palpable diffuse goiter	318	126	2	--	0.63	--
Group III. No palpable goiter present	22	24	1	--	4.5	--

It may be seen from these figures that the incidence of malignancy in individuals with adenomatous goiters (combining both sexes and with multiple adenomas as well as single adenomas) in this series is 6.94 per cent. In Horn's series the incidence was 5.5 per cent and in Ward's series[31, 58] 4.8 per cent. Cole and associates[10] reported an incidence of 7.2 per cent in nodular goiters and called attention to the fact that the incidence varies throughout the country, suggesting that geographic sites probably play a role in this variation. It is interesting to note in this connection that the incidence of 7.2 per cent reported by Cole very closely approximates our figure of 6.94 per cent, since both series come from the Great Lakes area, a well-known "goiter belt." Hinton and Lord,[30] on the other hand, found the incidence of cancer to be 7.6 per cent in 184 cases of clinically benign nodular goiters from the Atlantic seaboard.

The high incidence of thyroid cancer as reported in the literature has been questioned by some. VanderLaan[57] recently approached the problem in a different manner. He reviewed the autopsy records of half a century in the Boston City Hospital and concluded that thyroid carcinoma as a cause of death, at least, was extremely rare, having found only 5 instances in a series of 18,668 autopsies. He went further and compared the conclusions drawn from surgical material as reported by Cole and co-workers, with those of Jaffe drawn from autopsy material, both reports coming from the Chicago area. Applying Cole's findings to Jaffe's, it was concluded that thyroid carcinoma should be present in approximately 2 out of every 100 autopsies, whereas actually Jaffe found a ratio of 2 out of every 1,000 autopsies.

It should be emphasized that one might well expect significant statistical differences in comparing the incidence of malignancy in surgical material to a similar incidence in thyroid glands removed at autopsy. The selective forces producing these two groupings are obviously not identical.

The diagnosis of adenomatous goiter is made far more frequently on autopsy material than from clinical examination, and for obvious reasons. In this respect, it is interesting to consider a recent report by Martin.[42] He reviewed a series of 100 subjects, aged 45 years or over, coming to autopsy in East Anglia, where endemic goiter is not unduly prevalent. In 59 per cent he found diffuse colloid and nodular changes. In only 7 of the subjects were nodules detected by external examination. In 22, adenomas were found only on pathologic examination even though some were three-fourths inch in diameter.

With this in mind it was felt desirable to compare our clinical grouping as summarized in Table I with a subsequent grouping based on operative and pathologic findings as summarized in Table II. It is quite apparent from Table II that in this hospital at least not only are nodules overlooked at clinical examination, but not infrequently nodules are described where none exist.

TABLE II. COMPARISON OF CLINICAL GROUPING TO OPERATIVE AND PATHOLOGIC FINDINGS

Group I.	Clinically palpable nodular goiter (836)	
	(a) Multinodular (677)	
	Multiple nodules	641
	Single nodule	1
	No nodules found	35
	(b) Single nodule (159)	
	Single nodule	31
	Multiple nodules	126
	No nodules	2
Group II.	Clinically palpable diffuse goiter (444)	
	No nodules	317
	Multiple nodules	123
	Single nodule	4
Group III.	Clinically nonpalpable (46)	
	No nodules found	30
	Multiple nodules found	16

TABLE III. SEX INCIDENCE

	NO. OF PATIENTS TREATED SURGICALLY		CANCERS NO.	CANCERS PER CENT	PER CENT MALIGNANT
Females	1,033	(77.9%)	48	78.7	4.64
Males	293	(22.1%)	13	21.3	4.44
Total	1,326		61		4.6

When only the adenomatous goiters are considered, cancer was found in 1 of approximately every 15 females and 1 of every 11 males (Table I). While this limitation increases the apparent liability to malignancy among males with adenomatous goiters as compared to females, this difference is far less than reported elsewhere. Ward,[58] in a similar manner, found carcinoma once in every 17 males as compared to once in every 44 females. Tinker,[56] while confirming the fact that the total number of cancers was greater in females, found that given an equal number of goiterous men and women, the men were about twice as likely to develop cancer.

AGE DISTRIBUTION

More than five-sixths of the cancers in this series occurred in patients beyond the third decade, with a preponderance in the fifth decade. The youngest patients were three females aged 17 years, the oldest was a female aged 76. (See Table IV.)

That youth does not exclude the possibility of thyroid cancer has been well emphasized by many investigators.[33, 34, 46, 47, 53, 58] Kennedy[33] called attention to the fact that any palpable mass in the thyroid gland of a child should be suspected of possessing malignant qualities regardless of how innocent the mass might appear to be on clinical examination. Pemberton and Black[47]

TABLE IV. AGE DISTRIBUTION

AGE (YR.)	FEMALES	MALES	TOTAL
0-10	0	0	0
11-20	5	1	6
21-30	4	0	4
31-40	10	3	13
41-50	13	2	15
51-60	9	2	11
61-70	5	5	10
71-80	2	0	2
81-90	0	0	0
			61

reviewed the goiters in children 14 years of age or less encountered from 1908 through 1943 at the Mayo Clinic. During this period 53 children with nodular goiter were operated upon, and in 18 instances the nodularity proved to be due to cancer. This astonishing incidence of approximately 34 per cent malignancy emphasizes the great hazard presented by nodular goiter in children.

RELATION TO HYPERTHYROIDISM

It has been our experience in this hospital that hyperthyroidism is of no aid whatsoever in the differential diagnosis of malignant goiter. In an earlier report Coller[14] found abnormally high basal metabolic rates in 46 per cent of the individuals having malignant goiter. In the present series 26 per cent exhibited unequivocal symptoms of hyperthyroidism clinically and had elevated basal metabolic rates.

In general, this has been the experience of most authors on the subject. In Simpson's series[53] over one-half of the patients exhibited clinical hyperthyroidism. Pemberton[46] found the basal metabolic rate normal in 53.9 per cent, elevated in 33.5 per cent, and below normal in 12.6 per cent. In Cattell's recent series[8] 26 patients operated upon for hyperthyroidism were found to have unsuspected carcinoma.

In an excellent dissertation on primary carcinoma in exophthalmic goiter Goetsch[25] reported 9 instances of carcinoma associated with hyperthyroidism. That the origin of the neoplasms was demonstrably associated with minute adenomas in some instances (and, in fact, probably in all) in no way detracts from the fact that these are all instances of malignancy coincident with hyperthyroidism.

Clute and Albright[9] some time ago pointed out that hyperthyroidism may occur in patients with solitary discrete adenomas, and that enucleation of the adenoma alone may allay the manifestations of hyperthyroidism. Cope and co-workers,[17] have recently given striking proof of the truth of this contention by comparing the physiologic activity of the adenoma and the uninvolved thyroid gland tissue with respect to their ability to inactivate thyroid-stimulating hormone as well as their avidity for tracer doses of radioactive iodine. Puppel and associates[49] carried out similar investigations though with dissimilar results. However, they were dealing with diffuse disease, whereas Cope and co-workers were dealing with localized disease.

PATHOGENESIS

While the immediate cause of thyroid malignancy remains obscure, it is generally agreed that most, if not all, thyroid carcinomas originate in adenomatous foci. The term "thyroid adenoma," however, has been used rather loosely in referring to true adenomas and to nodular aggregates resulting from hyperplasia and involution. Clinically it is perhaps best to refer to all thyroid nodules by the term "nodular goiter" and reserve further differentiation for the histopathologist.

Warthin[60] believed that true adenomas are congenital disturbances of development and are never formed in extrauterine life. He further identified the true adenomas as always present at birth in the form of very minute, sharply circumscribed, encapsulated, atypical portions of thyroid tissue with abnormal vascular relations. He distinguished pseudoadenomatous nodules of involution from true adenomas by their lack of a definite capsule and their normal acinous and vascular relationships. He also believed that the majority of primary carcinomas of the thyroid, if not all, takes origin from true adenomas.

Lahey, Hare, and Warren[38] required the following criteria for identification of a true adenoma:

1. Complete encapsulation
2. Homogeneous texture, grossly and microscopically, throughout, with the exception of degenerative foci such as cysts, calcification, or fibrosis
3. Distinct variation of the tissue within the capsule from that outside the capsule
4. Evidence of compression of adjacent tissue by the nodules

They classified adenomas into four major groups, according to their differentiation as determined from the histologic appearance, as follows:

1. Embryonal adenoma
2. Fetal adenoma
3. Simple adenoma (including Hürthle cell adenoma)
4. Colloid adenoma

The embryonal type is the least differentiated, resembling the structure of the thyroid gland of early embryonic life, and made up of solid columns of small, compact polyhedral cells. Because of this pattern they are sometimes referred to as "trabecular adenomas."

The fetal type (as the term is used here) represents a more differentiated form than the embryonal type. On section the follicles resemble rosettes, are considerably smaller than those of the normal thyroid, and contain only a small amount of colloid. This type is sometimes referred to as "tubular adenoma."

The simple adenoma resembles more closely the structure of normal thyroid tissue; the acini are within normal range of size and are lined by cells varying from cuboidal to columnar. This type is sometimes referred to as "microfollicular adenoma."

The Hürthle cell type, as described by Lahey and co-workers, is characterized by the presence of acini lined with large, pale, clear acidophilic cells

with large prominent vesicular nuclei. This type is not recognized as a distinct entity by most writers. Eosinophilic staining is not infrequently seen by pathologists in a variety of conditions of the thyroid. Wilensky and Kaufman[63] suggested that the evidence at hand indicates a physiologic rather than an anatomic basis for the appearance of the so-called Hürthle cell in normal thyroid, and that the so-called Hürthle cell does not represent a distinct anatomic unit but rather a functional change, probably nutritive. They favored discarding the term "Hürthle cell tumor."

The colloid adenoma is the most differentiated type. On section the acini are greatly distended with colloid and the acinar epithelium is usually low cuboidal or flat. This type is sometimes referred to as "macrofollicular adenoma." Clute and Albright[9] classified all thyroid adenomas as either parenchymatous or colloid in form. The former are characterized by a quantitative preponderance of epithelial elements over colloid secretion and stroma; the latter are characterized by large follicle formation with abundant colloid and stroma. These authors pointed out that: "Different stages of development and differentiation, that is, both parenchymatous and colloid characteristics, may occur in different parts of a single adenoma."

Brenizer and McKnight[6] felt they could identify true adenomas from colloid inclusions by observing that with true adenomas they were able to strip the cellular mass more readily from the capsule. Hertzler[29] distinguished sharply between the bosselations of nodular goiter and true congenital tumors or fetal adenomas, stressing the independent origin of the latter and the fact that they never regress. Their ultimate fate, in Hertzler's opinion, is usually one of gradual degeneration and, less commonly, gradual progression to malignancy.

In contradistinction to true adenomas, the nodules most frequently found in adenomatous goiter are the result of repeated stimulation of the gland under the influence of various factors, followed by involution and colloid storage when the stimulus is withdrawn. A gland once stimulated to hyperplasia probably never returns entirely to normal. More often than not both the hyperplastic and involutionary sequences are not uniformly distributed throughout the gland. Areas begin to appear in which hyperplasia is greater and involution minimal, leading to development of irregularly scattered nodules of varying size. It is felt by many authors that such nodules are not in the nature of new growths either clinically or histologically, and are rarely, if ever, related to the origin of thyroid cancer.

The stimuli capable of initiating these cyclic changes in the thyroid are numerous. Physiologic stimuli of such nature are observed at puberty, during menses, and in pregnancy. The latter factors are cited frequently to account for the greater incidence of nodular goiter in females. Hyperplasia induced by infection and toxemia has been discussed by Cole, Womack, and Gray.[12] More recently various chemicals have been demonstrated to be capable of producing interesting and important forms of goiter. These have included methylated purines, thiocyanates, methyl cyanide, thiourea and various thiourea derivatives, the sulfonamides, and related compounds.[7, 11]

Womack and Cole,[65] realizing that it was possible to produce hyperplastic changes experimentally and at the same time to cause artificial involution by the use of iodine (or "natural" involution by withdrawing the stimulus), made some significant observations on the anatomic changes occurring in the thyroids of dogs subjected to such cyclic influence. Hyperplasia was induced by three forms of stimuli: (1) the production of infections; (2) the injection of methylated purines; and (3) the implantation of contaminated foreign bodies over a long period of time. By such means they were able to demonstrate the formation of small adenomas, formed apparently in proportion to the amount of fibrosis induced in the gland. Perhaps their most startling observation was: "Some of these nodules resembled the so-called fetal adenoma in such detail that while we cannot disprove the theory of embryonic rest, we are inclined at the present time to explain the presence of these nodules on the basis of morphologic changes as a result of a natural physiologic cycle. Although we have no proof that these adenomas were not already present in microscopic form before our experiments were started, we wish to emphasize the fact that in sections taken from several hundred normal dogs in the past few years, we did not encounter a single instance of adenoma." The reference to the theory of embryonic rests used here harks back to a theory propounded by Wölfler concerning the origin of true adenomas. It was Wölfler's contention (in accordance with Cohnheim's theory of the origin of tumors from congenital *Anlagen*) that adenomas had their origin from undifferentiated epithelial cell rests which had not been utilized in the formation of the normal gland and assumed an interacinar position. Some years ago Rienhoff,[50] employing painstaking wax models of the thyroid gland reconstructed from serial sections, concluded that what Wölfler observed was in reality tangential sections through the dome of an underlying follicle, giving the appearance of an isolated group of epithelial cells. He was unable to demonstrate the presence of fetal cell rests between normal adult follicles. It was Rienhoff's impression that the concept of fetal cell rests evolved from inexact methods, leading to inaccurate conclusions. Wölfler, working during the twilight of the nineteenth century, had to contend with poorly stained thick sections and without the advantage of serial cuttings.

Other theories concerning the origin of adenomas include the theory of dedifferentiation or reversion of the follicular cell to a more embryonic thyroid epithelial cell from which an adenoma might arise; also, the theory offered by Goetsch[25] that the true adenoma probably has its origin in certain cells which occur in the normal and hyperplastic follicle, and are known to have the characters of fetal or embryonic cells. Goetsch asserted that these occur, not uncommonly, singly or in pairs interposed between follicle-lining cells of the hyperplastic gland, and may be differentiated from the remaining cells of the follicle by their differences in size, shape, and in the nature of the mitochondria which their protoplasm contains.

The role of the so-called lateral aberrant thyroid nodules in the pathogenesis of thyroid cancer remains particularly controversial. It is now gener-

ally agreed that the thyroid gland of man is derived from one median and two lateral primordial structures.[44, 62] The median component originates as a diverticulum from the pharynx and migrates caudad along a path ventral to the pharynx. Almost from its initial appearance it is a bilobed structure and in the definitive position, reached during the seventh week, consists of two distinct lobes, one on either side of the midline, joined by a narrow isthmus. The point of origin remains marked by the foramen cecum. Developmental anomales related to this migration, such as lingual thyroids and thyroglossal duct cysts, are seen quite frequently. Far less commonly cancers have been observed to originate in such anomalies. Thus, squamous-cell carcinomas of presumable thyroglossal duct origin have been described,[46, 53] and in the series reported by Watson and Pool[61] primary cancer developed in lingual thyroid tissue in 3 instances.

The lateral components, according to Patten,[44] develop as small diverticula on the caudal face of the fourth pharyngeal pouch. These diverticula break loose from the fourth pouch and become incorporated with the lateral lobes of the median component as the latter reaches the posterior pharyngeal levels in its migration caudad. Some authors regard these diverticula as rudimentary fifth pharyngeal pouches. Others, convinced that they form true thyroid tissue, prefer to identify them as lateral thyroid primordia. Patten, though asserting that evidence in favor of the latter view is increasingly strong, suggests that until their significance is established beyond doubt, they might better be designated by the noncommital term "postbranchial bodies."

According to Weller[62] the median component, at the time of fusion, is composed of more differentiated tissue than the lateral contributions, but subsequently the median component undergoes little change except growth until both components are similar in appearance, whereupon the epithelial sheets undergo differentiation into follicles throughout the entire gland.

Single or, more frequently, multiple nodules are observed in the lateral cervical region (for the most part), which in microscopic section appear as papillary adenomas and occasionally frank papillary thyroid carcinomas. That there is considerable diversity of opinion regarding the origin, pathogenicity, and potential hazards of these lateral nodules has been adequately emphasized recently by Graham.[28] Lahey[37, 38] regarded them as lateral aberrant thyroid masses associated with developmental anomalies of the lateral primordia. He felt that they are all either malignant or potentially malignant, and consequently require radical surgical treatment followed by intensive radiation. In an earlier discussion Lahey[37] explained the occasional coexistence of a similar (papilliferous) nodule within the thyroid gland as probably representing a metastasis from lateral aberrant thyroid masses. More recently,[38] however, he has stated that such a coexistence could be explained on embryologic grounds without spread or metastasis in either direction. He would now regard the papilliferous nodule within the thyroid gland as representing a lateral aberrant nodule (fused with the thyroid) which had failed to undergo atrophy. Crile[18, 20] has summarized his experiences with respect to papillary

tumors in two excellent successive papers. In the earlier report Crile[18] regarded such tumors as multiple, primary, relatively benign or locally malignant lesions arising in some developmental disturbance associated with the lateral thyroid derivatives. While concurring with Lahey for the most part as to the origin of these tumors, even in this earlier report Crile considered x-ray therapy as ineffectual in their treatment, placing reliance on surgical removal.

Another view, as expressed by King and Pemberton,[35, 46] holds that "lateral aberrant thyroids" are in reality metastatic carcinomas in cervical lymph nodes, having metastasized there from a primary carcinoma in the homolateral lobe of the thyroid proper. Their evidence on the whole is rather convincing. They accordingly recommend radical block dissection of the neck with removal of the corresponding thyroid lobe whether or not a tumor can be felt or seen in that lobe at time of operation. They regard radiation therapy as of questionable benefit unless surgical removal of the diseased tissue has been incomplete.

Watson and Pool[61] reported several cases related to this problem which tend to support the view of King and Pemberton. They reported having seen extensive unilateral or bilateral cervical chains of carcinomatous thyroid tissue in several of their cases which first led them to suspect origin in multiple aberrant thyroid rests. However, when small unsuspected primary foci of carcinoma were found in the thyroid gland itself, they withdrew their original contention and in only one questionable instance could they suspect the primary disease as of aberrant thyroid origin.

Crile's most recent review of the subject[20] deserves particular attention. While not entirely abandoning his earlier theory that in some cases, at least, lateral cervical nodules are possibly multiple primary tumors of benign behavior, Crile later regarded these cervical nodules as probably representing metastases from a primary tumor of the thyroid. In 16 consecutive cases of papillary tumors of the cervical region, when the thyroid was carefully examined, a primary papillary neoplasm was found in the thyroid. Crile emphasized that the primary tumor may be very small, difficult to palpate, and occasionally not discovered until the gland is rotated out of its bed to expose the posteromedial surface, an area avoided by many surgeons. Unless the gland is explored thoroughly, a small primary may easily be left behind and lateral cervical tumors may continue to form; yet the primary may not enlarge appreciably over a period of many years. Crile again stated that in the few cases in which x-ray therapy had been given, the results were disappointing, whereas surgical excision of the primary and metastases had given excellent results.

Certainly the evidence that most of the so-called lateral aberrant thyroid tumors are in reality metastases is so convincing that all patients with ectopic thyroid tissue should have a thorough examination of the thyroid gland and perhaps a homolateral lobectomy in all instances.

Oddly enough in our series there was but one questionable instance of lateral aberrant thyroid nodules. Another possible consideration in the pathogenesis of thyroid carcinoma involves the prophylactic use of iodine.

Warthin[60] summarized his observations as follows: "... proliferation of the adenoma cells appears to result from over-iodinization. A peculiar hypertrophy of the adenoma is produced, and transitional stages between such hypertrophic proliferating adenomas and carcinoma have been observed. It is an open question whether the over-use of iodine may not stimulate the development of carcinomatous transformation of an adenoma in a patient possessing also the cancer-susceptibility constitution."

Moreover, since the introduction of thiourea derivatives in the management of hyperthyroidism, an even more disturbing correlation has possibly been observed. It is now generally believed that thiouracil ameliorates the symptoms of thyrotoxicosis by action outside of the gland. In fact, within the gland the associated changes closely resemble the histologic picture of the hyperplastic gland of preiodine days. One sees on cross section extreme hyperplasia with heightened epithelium, marked papillary infolding, and mitoses in the epithelial cells.[7, 23] Because of these cellular changes fears have been expressed of the possibility of inducing malignancy and it has been suggested that the drug be used only as a preliminary medication in preparing the patient for thyroidectomy, particularly in the presence of nodular changes within the gland.[22, 40, 45, 55]

Experimental studies carried out in Great Britain,[2, 3] and tersely summarized in a recent editorial,[22] would seem to carry the correlation beyond mere speculation regardless of how critical one wishes to remain. In 1941 Wilson and associates[64] reported the discovery of an extraordinarily powerful carcinogen, 2-acetoaminofluorene, which, when fed to rats, was capable of producing astonishingly frequent neoplasms in the organs and tissues of animals having a relatively low incidence of spontaneous occurence of tumors. Bielschowsky in Great Britain[2] not only confirmed their discovery but also carried it a step further in regard to thyroid cancers.[3] It had been observed in these experiments that none of the animals developed tumors of the thyroid gland despite the high incidence of neoplasms in other organs. With this in mind, Bielschowsky first induced intense hyperplastic changes in the thyroid gland by feeding his animals thiourea. Upon subsequently feeding them acetoaminofluorene, he was able to demonstrate the appearance of invasive epithelial tumors within the thyroid gland. Apparently antecedent or concurrent hyperplasia was a necessary and decisive factor in the production of these thyroid tumors.

The question has been editorially raised[22]: May not thiouracil similarly fortify the cancer-susceptibility factors (as yet unknown) leading to a higher incidence of malignancy in the human thyroid?

DIAGNOSIS

Most authors emphasize the fact that there are no reliable signs and symptoms upon which to make an early diagnosis of thyroid cancer.[24, 46, 53, 56, 58, 61] In the late cases the diagnosis may be only too obvious. Consequently, any diagnostic aids that might prove helpful in evaluating these cases are worthy of mention. A preoperative laryngoscopic examination should be

carried out on all thyroid patients to determine the condition of the vocal cords. Roentgenologic examination of the neck in both the anteroposterior and lateral planes, as well as a chest film, should be routine in all suspected cases. Tracheal compression or displacement may be demonstrated, as well as pulmonary metastases. Esophageal displacement or compression may similarly be demonstrated by the use of thick barium paste or mixture. Occasionally, esophagoscopy may be desirable to exclude primary malignant disease of the esophagus or to demonstrate secondary involvement. The possibility of distant metastases may call for a roentgenologic survey of the entire osseous system.

While it is true that it is impossible to make a clinical diagnosis of cancer in the very early instances, between this extreme and the opposite (where the diagnosis is obvious and prognosis correspondingly grave) there are certain clinical observations attributable to thyroid cancer. When the neoplasm is still confined within the capsule (except for occasional early metastatic foci), the only findings attributable to it are: (1) the recent development of a nodule not previously detected; (2) a history of recent enlargement in a pre-existing nodule; (3) the development of increased hardness and irregularity of a pre-existent nodule. In our series a history of goiter was elicited in all but 1 of the 61 cases. The enlargement was of relatively recent origin (three weeks to one year) and exhibited relatively rapid growth in 7 instances. The enlargement was of long duration in 48 patients, with a history of gradual recent enlargement in 19 and relatively rapid recent enlargement in 29. Goiter of long duration with no history of recent enlargement was obtained in the other 5.

Significant hardness of the gland was observed in 12 instances in this series; it was associated with fixation in 8 cases and present alone in 4.

Once penetration of the capsule occurs, fixation to surrounding structures leads to loss of mobility and other manifestations depending on what structures are pressed upon or infiltrated.

Fixation was observed in 11 instances, in 3 of which no mention was made of any unusual hardness being present. Penetration into the tracheoesophageal sulcus is likely to produce hoarseness by pressure upon, or involvement of, the recurrent laryngeal nerve. Demonstrable cord paralysis is in general a grave sign.

Ward[58] stated that the clinical triad of hoarseness, fixation, and hardness, commonly regared as cardinal signs of cancer of the thyroid gland, can all be found in association with benigh nodular goiter as well. Pemberton[46] asserted that while a benign thyroid tumor may occasionally produce interference with vocal cord function, as manifested by a hoarse brassy voice, it is extremely uncommon for such a tumor to produce the fixed vocal cord of recurrent laryngeal paralysis. Pemberton regarded the combination of hoarseness and fixed cord, in the absence of syphilis, aortic aneurysm, or mitral stenosis, as almost pathognomonic of thyroid cancer, irrespective of size, contour, or consistency of the gland. Hoarseness was present in 12 patients from our series, 7 of whom also showed unilateral vocal cord fixation. Of this latter group,

5 were dead within seventeen months, and the remaining 2 are alive and apparently free of carcinoma 5 and 5½ years later. Of the 5 patients exhibiting hoarseness alone, one did not have a laryngeal examination, 3 showed no vocal cord paralysis, and one with normal vocal cords exhibited definite tracheal compression below the vocal cords.

Dyspnea and dysphagia are two commonly mentioned pressure symptoms associated with thyroid enlargement. Dyspnea is so frequently associated with benign thyroid enlargement that of itself it has little or no significance in regard to malignancy. Dysphagia, on the other hand, deserves more serious attention. It is not uncommon to find patients with tremendous benign goiters complaining of considerable dyspnea but having no difficulty whatsoever with swallowing. Tinker[56] found dysphagia present twice as frequently in malignant as in benign goiters. Dyspnea alone was present in 16 of our cases; dysphagia alone in 3; and the combination of dyspnea and dysphagia in 6.

Simpson[53] described the occurrence of neuralgic pains originating in the neck and radiating upward toward the ear and downward into the arm and shoulder as important early manifestations of cancer, rarely experienced in benign goiter. Tinker,[56] on the other hand, regarded such manifestations as of no diagnostic value, stating that in his experience such pain is approximately equally common in benign lesions. Three patients in our series complained of pain of this type.

Less commonly mentioned are symptoms associated with pressure upon, or invasion of, the cervical sympathetic or vagus nerves.[24, 53] In the former situation one may observe any or all of the classical components of a Horner's syndrome, while in the latter situation one might expect to observe disturbances in cardiac rate and rhythm.

Calcification deserves mention for at least two reasons. In the first place, calcareous infiltration produces a hardness clinically indistinguishable from carcinoma and its incidence is said to be at least five times as great.[56] Second, the simultaneous occurrence of calcification and cancer is not uncommon.[53, 58] In Ward's experience both are not infrequently found in the same nodule.[58]

Aspiration biopsies have proved worth while as a means of establishing an accurate preoperative diagnosis in the hands of Watson and Pool.[61] They emphasized that a negative biopsy means absolutely nothing. In 74 cases where aspiration biopsy was employed, they were able to obtain a positive diagnosis in 62 instances. They felt (and one must concur) that a preoperative diagnostic procedure which yields positive results in 83 per cent of the cases is of definite value.

Aspiration biopsies have not been used in our clinic; however, our experience with frozen section examination at time of operation has been disappointing. Frozen section examination was requested in 6 of our cases and proved misleading in 5. There is no attempt made here to minimize the difficulties set before even the most competent and experienced pathologist since accurate definitive diagnosis may be impossible from such material by frozen-section examination. The experienced surgeon, as emphasized by Wat-

son and Pool, impressed with the possibility that he is dealing with thyroid cancer, should not hesitate to proceed with a suitable operation in the best interests of the patient, irrespective of the frozen-section report.

In the differential diagnosis of lesions most likely to be mistaken clinically for thyroid cancer, or vice versa, one should consider: (1) Benign nodular goiter, (2) sudden hemorrhage, (3) acute thyroiditis, (4) chronic thyroiditis (Hashimoto and Riedel types), (5) calcareous infiltration, and (6) chronic infective granulomas.

In this series, of the 56 epithelial neoplasms the diagnosis was made clinically in only 8 instances; malignancy was clinically suspected and confirmed at operation in 8 instances; it was not suspected both clinically and at operation in 39 instances; and in 1 instance malignancy was not suspected clinically, was not found in the specimen removed at operation, but found in the remnant left behind when the patient came to autopsy (postoperative death).

All 5 of the cases diagnosed ultimately as sarcomas were either diagnosed clinically as cancer or were strongly suspected of cancer. This diagnosis was unequivocally made clinically in 3 instances, and confirmed at operation in the others. In no instance was the sarcomatous nature suspected until the microscopic reports became available.

The microscopic diagnosis of thyroid cancer has long been a source of contention among pathologists. The nature of a tumor that exhibits destructive infiltrative growth, or that gives rise to distant metastases, one that recurs following excision or kills the host, is now rarely in doubt. Differences of opinion arise in respect to the interpretation of early malignancy.

Graham,[26] after a painstaking review of the problem, emphasized the importance of blood vessel invasion as not only an absolute criterion but, indeed, the only criterion of malignancy in respect to some encapsulated nodules.

Warren[59] found that in 1,080 cases of surgically removed adenomas not showing blood vessel invasion, none gave evidence of malignancy from 2½ to 7 years following operation. Whereas of 34 patients who did show blood vessel invasion, 2 died (10 months and 2½ years following operation) of local recurrence and multiple metastases.

While no one questions the accuracy or the significance of Graham's observations, many experienced pathologists and clinicians alike have long felt that such criteria are too rigid and that the presence of blood vessel invasion is not necessary for the accurate diagnosis of thyroid malignancy.

Pemberton[46] called attention to the enlargement of the nucleolus (long recognized as a characteristic feature of malignant cells), and described a nucleolar-nuclear ratio that may be employed as a measurable criterion of malignancy.

The pathologists in our hospital have always felt that the diagnosis of thyroid cancer should be based on the same criteria that are applied to cancer of all other organs and tissues. These are, namely, loss of differentiation, hyperchromatic nuclei, number of mitotic figures, presence of atypical mitotic figures, and infiltrative growth.

Some years ago in a personal communication to Coller[14] these criteria were epitomized by Warthin as follows:

> The usual criteria of malignancy: changes in cell type and staining reaction, alteration in function as shown by the disappearance of colloid, abnormal architecture, infiltration of surrounding tissue, inflammatory reactions about the neoplasm, extension into lympathic and blood vessels, abnormal retrogressive changes in the parenchymatous cells of the new growth, and finally metastases—all of these apply to the diagnosis of thyroid carcinoma as in malignancy in other organs. To any one familiar with the cyclic histologic changes in the thyroid, particularly those associated with exophthalmic goiter, the differential diagnosis of malignancy using the ordinary criteria presents no especial difficulty in the case of the great majority of thyroid cancers. It must be remembered, however, that an experienced pathologist may mistakenly diagnose the typical parenchymatous hypertrophy of exophthalmic goiter as adenocarcinoma or papilliferous adenocarcinoma. Such mistakes are by no means rare. Only in the case of malignant adenoma colloids in which the structure of the neoplasm may closely imitate that of normal gland structure is there likely to be any difficulty in the diagnosis. When metastases of such malignant adenomas are found in the bones or in other tissues, the fact that they are out of place is sufficient for the diagnosis. A study of numerous blocks from the primary lesion in the thyroid will always reveal local evidence of malignancy, particularly the invasion of normal thyroid tissue by the atypical acini and their extension into the lymphatics and veins in the trabeculae of the gland. Graham's criterion of growth into blood vessels would apply in this case, but in the great majority of cases of thyroid cancer such a criterion of malignancy is not necessary to the correct diagnosis, and in many cases extension into the blood vessels will not be found. It must be emphasized here in this connection that hematogenous metastasis is not common in cases of thyroid carcinoma until cervical and mediastinal nodes have reached a large size. The early hematogenous metastases into bones and lungs are relatively rare.

CLASSIFICATION

The classification of thyroid neoplasms has been no less controversial than the microscopic criteria of malignancy. The practical value of any classification would appear to repose in how closely it correlated the recognizable histopathologic features with the clinical course of the disease. Perhaps too much emphasis has been placed on classification since, as is true of so many neoplasms, it is not uncommon to find several types represented in different areas of the same specimen. Moreover, imperceptible gradations from one type to another as well as intermediate forms constitute common findings.[9] (In such cases it is the usual practice arbitrarily to classify on the basis of what is believed to be the most malignant type represented.)

The classification used by Lahey, Hare, and Warren[38] is one frequently adopted by others:[31, 43]

Group I: Low or Potential Malignancy.

(1) Adenoma with blood vessel invasion.
(2) Papillary cystadenoma with blood vessel invasion.
  (a) Originating from thyroid.
  (b) Originating from aberrant thyroid.

Group II: Moderate Malignancy.
(1) Papillary adenocarcinoma.
(2) Alveolar adenocarcinoma.
(3) Hürthle cell adenocarcinoma.
Group III: High Malignancy.
(1) Small-cell carcinoma (carcinoma simplex).
(a) Compact type.
(b) Diffuse type.
(2) Giant-cell carcinoma.
(3) Epidermoid carcinoma.
(4) Fibrosarcoma.
(5) Lymphoma.

The classification used by Pemberton[46] is far more simple:
(1) Papillary adenocarcinoma.
(2) Adenocarcinoma in adenoma (malignant adenoma).
(3) Diffuse adenocarcinoma.
(4) Epithelioma.
(5) Sarcoma.

Watson and Pool[61] divided thyroid cancers into six major groupings. A further breakdown of each group is afforded on the basis of grading.

Group I. Papillary adenocarcinoma.
Group II. Small alveolar and solid large-cell adenocarcinoma.
Group III. Spindle- and giant-cell carcinoma.
Group IV. Small round-cell carcinoma.
Group V. Metastasizing struma.
Group VI. Lymphosarcoma.

Singularly simple and eminently practical is the classification used by Ward.[58] It is based on prognostic and therapeutic criteria:

Group I. Papillary carcinomas.
Group II. Malignant adenomas.
Group III. All others, including scirrhous, small-cell types, undifferentiated carcinomas, and those which display a sarcomatous tendency.

A somewhat different type of classification is one proposed by Portmann.[48] It is based essentially on the extent of involvement. A notable feature of this classification is the fact that it affords a common denominator applicable to most popular classifications, and thus affords a basis for comparative study. In brief, the classification is as follows:

Group I. Cases diagnosed only after microscopic examination.
Group II. Cases in which diagnosis is suspected on the basis of the patient's age, recent rapid enlargement, or discovery at operation (tumor still localized within the capsule of the gland).
Group III. Cases in which there is clinical or pathologic evidence that the neoplasm is invading or extending outside the capsule of the gland, but without evidence of distant metastases.
Group IV. Cases with evidence of distant metastases.

In the present series there were 56 epithelial neoplasms or carcinomas and 5 sarcomas, an incidence of 91.8 per cent and 8.2 per cent, respectively. The 56 epithelial neoplasms in our series are according to Portmann's classification in Table VI.

TABLE V. DISTRIBUTION OF PATHOLOGIC TYPES OF FIFTY-SIX EPITHELIAL NEOPLASMS

	NUMBER
Group I. Medullary Carcinoma (23)	
(a) Diffuse type	11
(b) Hypernephroid type	8
(c) Malignant adenoma	4
Group II. Adenocarcinoma (29)	
(a) Diffuse type	5
(b) Malignant adenoma	24
Group III. Scirrhous Carcinoma (4)	
(a) Ordinary type	2
(b) "Carcinosarcoma" type	2

TABLE VI. DISTRIBUTION OF FIFTY-SIX EPITHELIAL NEOPLASMS ON THE BASIS OF PORTMANN'S CLASSIFICATION*

Group I.	30
Group II.	11
Group III.	9
Group IV.	5 (plus 1)*

*One case not classified here because of the possibility that the regional foci were lateral aberrant thyroid tissue rather than metastases.

It is frequently asserted that most, if not all, so-called "sarcomas" of the thyroid are in reality highly anaplastic carcinomas. Uncertainty stems from the close microscopic resemblance of highly anaplastic epithelial cells to equally anaplastic supporting tissue cells.

That sarcomas of the thyroid do occur, however, cannot be denied since there has been a sufficient number reported whose sarcomatous nature cannot be denied.

Lahey and associates[38] accepted but one criterion in identifying fibrosarcomas, namely, that of a typical sarcoma, the cells of which show definite collagen or fibroglial fibrils. Pemberton[46] thought that the incidence of sarcoma as reported in the literature is far too high. In his series of 774 thyroid cancers, the diagnosis of sarcoma was established in but 4 instances. Batts[1] reported an osteogenic sarcoma arising in the thyroid and found 7 other cases reported in the literature. One of these occurred in the series reported by Pemberton.[46] Joyce and co-workers[32] reported a liposarcoma of thyroid origin. Simpson's[53] series contained 5 sarcomas, a proportion of 1 sarcoma to 10 carcinomas.

The 5 sarcomas in our series were all diagnosed as the spindle-cell type.

METASTASES

Metastases were observed in 9 instances in this series. The most frequent site of involvement was the lungs, pulmonary metastases being observed in 6 cases. Other sites included cervical lymph nodes, the mediastinum, skull, pelvis, brain, and adrenals.

Pemberton[46] and Horn and co-workers[31] found the highest incidence of involvement to be in the cervical lymph nodes. Pemberton also found a marked predilection of papillary adenocarcinoma to spread to cervical lymph nodes.

Ward[58] emphasized the fact that following removal of the primary tumor, pulmonary metastases will occasionally lie dormant for many years. One of his patients was alive and in apparent good health 13 years after the lungs had been observed to be riddled with miliary nodules. Moreover, numerous examples can be found in the literature of patients living in apparent good health for many years following removal of isolated metastatic nodules and subsequent thyroidectomy. Ward[58] pointed out that in some cases the primary lesion may be microscopic in size and identified only after serial section of the entire gland. Failure to recognize this fact has probably been responsible for the not infrequent reference to so-called "benign metastasizing goiter" in earlier reports. Simpson,[54] some years ago, made a comprehensive study of the subject and proved quite conclusively that there was no basis in fact for the contention that such foci represented aberrant thyroid tissue. He urged that the term "benign metastasizing goiter" be abandoned as confusing and erroneous.

Metastases to the thyroid gland itself are extremely uncommon. In the present series there was 1 instance (not included in our total) in which a thyroid nodule proved to be a metastasis from a breast carcinoma. Linton[41] recently reported a case in which a hypernephroma metastasized to the thyroid gland. He was able to find 15 other such cases in the literature. It is interesting, in this connection, to observe that Simpson, in reviewing the problem of primary thyroid carcinoma resembling hypernephroma, called attention to the fact that such tumors, on occasion, have been erroneously interpreted as metastases to the thyroid.[52]

PROGNOSIS

As pointed out by Watson and Pool,[61] in considering the end results and prognosis of thyroid carcinoma, it is well to speak of "survival" rather than "cure" rates. This is necessarily so since it is well known that the disease may exhibit recurrence or metastases long after apparent cure. Watson and Pool reported 2 instances of total recurrence 16 years following treatment. Rosh and Raider[51] also reported a case in which metastases appeared 16 years after operation. Numerous similar examples are readily found in the literature.

Ward[58] based prognosis upon three principal factors. (1) the time of diagnosis, (2) the pathologic pattern, and (3) the presence of metastases. Deaths occured in direct proportion to the ease of diagnosis. Thus, there was a 20 per cent 5 year survival rate in those diagnosed or suspected preoperatively, and an 80 per cent 5 year survival in cases in which the diagnosis was first made by the pathologist.

In Ward's series the presence of a papillary pattern offered by far the best prognosis; indeed, the degree of malignancy could apparently be estimated by the extent of departure from this pattern.

Kroger,[36] in reviewing carcinomas forming the spindle-cell pattern, came to the conclusion that this particular variety was seemingly completely resistant to both surgical and radiation forms of therapy.

In the present series all 5 of the patients upon whom the diagnosis of sarcoma was made were dead within 1 year; indeed, 4 of them were dead within 4 months following operation.

The survival rate of the 56 patients having epithelial neoplasms was analyzed on the basis of Portmann's classification:

Group I. Included 30 cases. At the time this analysis was made, 22 of this group were still living; 8 had died. Of the 22 living, 5 were alive and free of recurrence for a period of 10 years or longer; 14 for a period of 5 years or longer; the remaining 3 had an elapsed survival time of less than 5 years. Of the 8 who had died, there was a question of recurrence in but 1 instance. This patient died elsewhere some 7½ years following operation, and no autopsy was obtained. All others died of causes other than cancer.

Group II. Included 11 cases. At the time this analysis was made, 7 of this group were still living; 4 had died. Of the 7 living: 1 was alive and free of recurrence for a period of 11 years; 4 for 5 years or longer but less than 10 years; and 2 for less than 5 years. Of the 4 who had lived, there was 1 instance of death by violence, while the remaining 3 died of recurrence with distant metastases (7 months, 3½ years, and 5 years respectively following operation).

Group III. Included 9 cases. At the time of this analysis, 3 of this group were alive; 6 had died. Of the 3 living survivors, all have passed the 5 year period.

Of the 6 who had died, there was 1 instance of death by cerebral hemorrhage without evidence of recurrence. The remaining 5 died of obvious recurrence within 9 months following operation.

Group IV. Included 5 cases, 1 case being purposely omitted since it was the only instance in this series of a possible lateral aberrant thyroid origin. If the cervical nodules are regarded as metastases, then this case would belong in Group IV, and the total number of cases would be 6. The patient in question was alive and well 5 years following surgical removal of the cervical nodules and the homolateral lobe. Considering these 5 cases, at the time of this analysis only 1 was living; 4 had died. The lone survivor had passed the 4 year period but had a probable pelvic metastasis. The 4 deaths were all due to obvious recurrent thyroid neoplasm. All were dead within less than 3 years following treatment. It is interesting to note that 1 case showed at autopsy multiple miliary carcinomatous nodules throughout both lungs which had been observed on roentgenologic examination just before death. It is quite apparent from this analysis that Portmann's classification (based on the extent of the disease) has definite prognostic significance. Horn and associates[31] reported an essentially similar experience in their series. The operative mortality in this hospital was determined for the last 3 year period. The operative mortality for

all thyroidectomies (including hopeless malignant goiters where surgery was limited to lifesaving traceal decompression) was 1.56 per cent; if thyroid cancer is excluded, the operative mortality was 0.3 per cent.

TREATMENT

The evaluation of operability and the extent of the operative procedure to be undertaken will always vary with the skill and experience of the surgeon.

Pemberton[46] felt that operability depends on the extent of the local invasion of the primary lesion and the absence of distant metastases. Tumors that are completely fixed should not be operated upon since the risk of extirpation would be out of proportion to the amount of benefit one could hope to derive. When mobility is limited, in Pemberton's opinion, exploration is justifiable even though the tumor cannot be completely removed, since this permits direct radium application to the fragments left. In his experience this procedure was particularly effective in the treatment of papillary carcinomas. Pemberton cited several instances of individuals living many years without evidence of recurrence following treatment by incomplete excision supplemented with radiation therapy. He regarded this combined form of therapy as the most effective form of treatment available, depending on the type and grade of malignancy.

At the Lahey Clinic postoperative irradiation is used in all cases of thyroid cancer regardless of the pathologic type or the extent of involvement.[38] In the management of so-called lateral aberrant thyroids Lahey and coworkers[38] and, more recently, Cattell,[8] recommended radical neck dissection plus removal of the homolateral thyroid lobe. With regard to discrete adenomas, Lahey felt that it is unnecessary to do more than a complete excision of the adenoma with its capsule intact. When erosion of the capsule and involvement of the parenchyma have occurred, the entire lobe and isthmus together with the contained neoplasm are removed intact. The attitude of the Lahey group toward the management of more extensive neoplasms has recently become more optimistic.[8] In former years they were content to prove the diagnosis by biopsy and rely on radiation therapy. At present they believe that as much of the neoplasm as possible should be removed, tracheotomy performed, and intensive postoperative irradiation therapy instituted. Radical neck dissection is eschewed in extensive cases. Irradiation therapy is started as soon as the patient's condition warrants it, usually within one week. They have felt that there need be no concern regarding failure of healing, even after a 5 day period has elapsed. While on the whole results in these advanced cases continue to be poor, there is an occasional long survival.

As stated previously, Crile[18] regarded papillary tumors of the thyroid and of lateral aberrant thyroid origin as singularly benign in most instances. He preferred to treat these lesions by surgical excision. Moreover, local recurrences following incomplete operation are also treated by re-operation rather than by irradiation therapy.

In this connection, it is interesting to note Graham's[27] experiences with local recurrences in the veins of the neck without detectable evidence of distant

metastases. The local recurrence presumably arises in a remnant of tumor tissue reposing in an isolated venous segment that was overlooked at the original operation. The most effective treatment of such recurrences proved to be a properly planned surgical removal. Radium and roentgen therapy proved ineffectual both in preventing such recurrences and in curing them. The radical operation for malignant thyroid tumors described by Crile and Crile[21] was designed, in part at least, to minimize or prevent such recurrences and is a well-planned procedure.

Ward[58] considered the therapeutic problem from three phases: prophylactic, definitive, and palliative. Simple enucleation of adenomas is frequently regarded as adequate prophylactic treatment. However, Ward confessed his regret upon occasion at not having originally performed lobectomy or subtotal thyroidectomy upon receiving the pathologist's report of malignancy in the enucleated specimen. In selected instances of this kind Ward believed the surgeon to be justified in immediate reoperation to remove the involved lobe and suspected soft tissue in the neighborhood. In one such case carcinoma was demonstrated in the specimen removed at the second operation, and the patient remained well for over 15 years. In instances where carcinoma is suspected preoperatively, Ward recommended that a radical operation be planned, employing the type of operation recommended by Crile and Crile. Regardless of the type of anesthetic employed, Ward recommended the use of an intratracheal catheter with inflatable cuff. Mediastinal extension in his experience often proves to be an unsurmountable obstacle to complete removal of the tumor. He has found irradiation therapy to be of little value except for papillary carcinomas and in a small number of malignant adenomas. In dealing with large and small cell anaplastic carcinomas or the so-called carcinosarcomas, he found both surgery and irradiation ineffectual. Metastases, if not too widespread and fulminating, are given a trial of irradiation; the papilliferous types usually respond well, whereas malignant adenomas show little response. Local recurrent nodules are removed surgically.

Horn and associates[31] favored a combination of surgery and irradiation in the treatment of lateral aberrant nodules. Surgical removal has been the initial treatment of choice. In general, they have found irradiation therapy of value, though recognizing that permanent cures may never be assured by this means. It has been their policy to wait 2 to 3 months following surgery before initiating irradiation therapy in order to permit physiologic repair to take place. When the surgical procedure is limited to simple exploration and biopsy, irradiation is started immediately. In treating patients with pulmonary metastases, they urged extreme caution since in their experience the presence of metastatic carcinoma renders the patient especially susceptible to radiation pneumonitis. Their data support the opinion of Portmann that routine postoperative irradiation therapy does not clearly benefit the patient with malignant adenoma or papillary carcinoma which has been discovered only on pathologic examination and is confined within a capsule. Their clinical experience led them to believe that all other patients should receive irradiation.

Watson and Pool[61] described a technique of radical thyroidectomy combined with neck dissection which is carried out under local Novocain infiltration and cervical nerve block anesthesia. In a series of 12 such radical procedures there was no death. Mention has already been made of their use of aspiration biopsies in planning the extent of the surgical procedure. Their experience led them to conclude that thyroid cancer cannot be classed as a radiosensitive lesion. They felt that it responds best to a combination of surgery and interstitial radiation in the form of gold-filtered radon seeds. In far-advanced cases palliative operative procedures for temporary relief of dyspnea and dysphagia were attended by a high operative mortality; for example, tracheotomy was followed by death in 50 per cent of 14 cases.

Rosh and Raider[51] discussed irradiation therapy. They treat all thyroid cancers to skin tolerance and repeat the series, if the skin is in satisfactory condition, within 6 to 8 weeks. Residual tumors following the second series are treated by gamma rays in the form of a radium pack or a collar containing radium tubes.

Several authors have observed that occasionally a lesion previously considered inoperable becomes operable following palliative irradiation therapy.[31, 38, 58]

Because of the relatively high incidence of unsuspected malignancy in apparently benign nodular goiters, the early removal of all such goiters is strongly recommended in this hospital. Moreover, additional considerations have been cited frequently enough to make us seriously doubt that any nodular goiter should ever be regarded as innocent.[9, 10, 13, 15, 16] Among these additional considerations the ones most frequently mentioned are: the development of pressure symptoms, the development of hyperthyroidism (which appears in particularly significant instances after the third decade), and the definite cardiovascular damage which appears in at least one-quarter of those with hyperthyroidism and in a smaller but appreciable number of those with normal metabolism. In the group with normal metabolic rates the development of symptoms is notoriously insidious. However, the improvement in health of many of these patients following thyroidectomy has convinced many clinicians that unrecognized toxicity or an altered secretion is frequently associated with nontoxic nodular goiters. The basal metabolic rates following removal of nontoxic goiters remain essentially what they were prior to operation.

In general, the stage and extent of the disease determine the magnitude of the surgical procedure carried out. It has been the practice in this hospital to carry out relatively radical subtotal thyroidectomies on all nodular goiters. Enucleation procedures are generally eschewed since it has been our experience that adenomas are usually multiple, and it is extremely difficult to palpate intraglandular nodules. In consequence of this attitude, the initial operation frequently proves sufficient for the not inconsiderable number of unsuspected carcinomas that are discovered on microscopic examination. If any question of completeness of the operation exists, there is no hesitation to reoperate promptly, at which time a total homolateral extirpation is carried out on the involved side and a search made for any evidence of spread.

In the presence of extracapsular invasion a radical unilateral neck dissection and total removal of the involved lobe are carried out.

In dealing with clinically obvious cancers (which may or may not have regional lymph node metastases), the patient is operated upon with the intention of radical gland removal combined with block dissection of the involved side.

When the lesion is considered inoperable, as much of the neoplasm as possible is removed. Every effort is exerted to clean the trachea. Removal of such neoplastic masses may occasionally be facilitated by use of the electrosurgical unit.

While our attitude in regard to the treatment of thyroid carcinomas has been to consider them a surgical problem, irradiation therapy enters the picture when removal is incomplete or in the event of inoperability. When irradiation is used, in most instances, treatment is applied through two lateral fields, treating one field a day, alternating between the two fields. The usual dose amounts to about 3,000 roentgens (as measured in air) to each of the two fields. The radiation is usually given at the rate of 200 roentgens per day. Two hundred K.V. filtered radiation of H.V.L. 1.0 mm. Cu is used at a distance of 50 cm.[39]

Before instituting irradiation therapy, microscopic examination of at least a biopsy specimen is mandatory.

The possibility of postoperative respiratory obstruction occurring either following surgery or during the course of postoperative irradiation therapy must be kept in mind. Tracheotomy is strongly advised upon completion of the operation if there is the slightest doubt about the patient's breathing, rather than waiting until cyanosis makes it mandatory. It is also recommended for patients judged inoperable in whom intensive postoperative irradiation therapy is contemplated, even though partial removal of the neoplastic mass leaves the trachea relatively free.

SUMMARY AND CONCLUSIONS

The incidence of malignancy in all surgically treated goiters during a 10 year period was 4.6 per cent (61 malignant neoplasms in 1,326 cases).

Of the 1,326 surgically treated goiters, 1,033 (78 per cent) were in females and 293 (22 per cent) were in males.

Thyroid cancer was found in 48 females (79 per cent of the total) and in 13 males (21 per cent of the total); or a sex incidence of 4.64 and 4.44 per cent, respectively.

The incidence of malignancy in individuals with clinically nodular goiters (considering both sexes and single as well as multiple nodules) was 6.94 per cent.

Among females with clinically nodular goiters the incidence of malignancy was 6.5 per cent; among males 9.1 per cent. Considering multinodular glands alone, the incidence of malignancy for females was 6 per cent and for males 9.56 per cent. Considering glands with only a single nodule found on clinical examination, the incidence of malignancy was 8.4 per cent among females and 7.14 per cent among males.

In individuals having clinically diffuse palpable goiters the incidence of malignancy among the females was 4.5 per cent; again there were no cancers in the males of this group.

Thyroid nodules were frequently overlooked during clinical examination and occasionally described where subsequent examination by both the surgeon and the pathologist failed to confirm their presence.

Youth does not minimize the likelihood of thyroid malignancy.

The presence of hyperthyroidism in no way excludes or minimizes the possibility of malignancy. Clear-cut hyperthyroidism was present in 26 per cent of the patients in this series.

While the immediate cause of thyroid malignancy remains obscure, most, if not all, thyroid cancers seem to originate in adenomatous foci. In all but one of the patients in this series a history of previous goiter was elicited.

In patients with clinically palpable nodular goiters, thiouracil (and similar compounds) should be used only as a preoperative measure, primarily because of the high incidence of malignancy in such goiters and secondarily because the question has been raised that such drugs are in themselves carcinogens or may enhance cancer-susceptibility.

There are no reliable signs and symptoms by which the diagnosis of early thyroid cancer may be established. In clinically suspicious lesions the presence of hoarseness and demonstrable vocal-cord paralysis constitutes ominous supportive evidence of advanced neoplasia.

Frozen section examination at the time of operation is unreliable and occasionally misleading, and consequently should not influence the surgeon's judgment too seriously.

The classification of thyroid cancers likewise continues to vary in different centers, although fortunately those most frequently adopted by others are characterized by increasing simplicity. Portmann's classification, based on the amount of infiltrative growth, affords a common denominator applicable to most of the popular classifications and thus allows a basis for comparative study.

In this series of 61 cancers, 56 were classified as epithelial in origin and, therefore, carcinomas, and 5 were identified as sarcomas, an incidence of 91.8 and 8.2 per cent, respectively.

All of the sarcomas were designated as spindle-cell type. While this high incidence of sarcomatous lesions is open to question, at least one of these cases offered strong supportive evidence of its sarcomatous nature in the form of not only hyaline change but also cartilage formation.

Whatever the true nature of these lesions might be, the diagnosis of thyroid sarcoma offers, categorically, an extremely grave prognosis.

The prognosis for epithelial neoplasms is far better and in many instances quite optimistic.

Our attitude in regard to the treatment of thyroid carcinomas has been to consider them as surgical problems with irradiation therapy entering the picture when removal is complete, or in the event of inoperability.

Our attitude in respect to nodular goiters has been to regard them as having sufficiently high malignant potentialities to be regarded as precancerous lesions. And since the operative mortality (excluding cancers) for thyroidectomy is merely 0.3 per cent, we strongly urge thyroidectomy for all such patients unless serious contraindications exist.

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Book Reviews

Sterility and Impaired Fertility. By Cedric Lane-Roberts, C.V.O., M.S., F.R.C.S., F.R.C.O.G., Gynecological Surgeon, Royal Northern Hospital, London; and associates. Pp. 400, with many illustrations. New York, 1948, Paul B. Hoeber, Inc.

This is the second edition of a well-known monograph dealing with human fertility. The authors are gynecologists from London and Glasgow, an "andrologist," an assistant in a London fertility clinic, and B. P. Wiesner, the distinguished biologist who has done so much work in the field of human reproduction. The book is designed for the general practitioner and has an attractive practical approach. It is nicely organized and surprisingly complete for a small monograph. The whole field of male and female infertility is covered and both clinical and laboratory approach, with practical and theoretical considerations, are presented in detail. It is an authoritative presentation with little to which one can take exception. It is the kind of volume that one can easily use in the actual practical study and treatment of a clinical problem.

Altogether, it is at least as good a practical guide as is presently available and is to be recommended for such use.

Atlas of Roentgenographic Positions. By Vinita Merrill, while Educational Director, Picker X-Ray Corporation. Ed. 1. Cloth. Two volumes, Pp. 708, over 1,500 illustrations. St. Louis, 1949, the C. V. Mosby Company. $30.

This Atlas represents a most complete assemblage of known roentgenographic positions in literature and is written for the student, technician, or doctor desiring to obtain a comprehensive and fundamental knowledge of this field. The Atlas consists of two volumes of 708 pages, which include over 1,500 illustrations. The first volume is comprised of sections dealing with preliminary steps in roentgenography, general anatomy, and anatomic terms, upper extremity, lower extremity, shoulder girdle, bony thorax, pelvic girdle, spinal column, and a glossary of medical and anatomic terms. The second volume presents the skull, sinuses, cerebral pneumography, facial bones, mouth, neck, body cavities, thoracic viscera, digestive system, excretory system, and female reproductive system. At the end of each volume is an extensive bibliography of the material contained within if further study is desired.

The text is concise and well written. The printed material is large enough to be easily read and the illustrations of the positions used and the resultant roentgenograms are exceptionally clear and accurate. A helpful feature for the student and technician is the discussion and the line illustrations of the anatomy which precede each section.

This is highly recommended as an excellent reference book for all of the standard positions, and almost all of the more unusual and specialized positions, used in roentgenographic positioning.

Clinical Aspects and Treatment of Surgical Infections. By Frank L. Meleney, M.D., F.A.C.S., Associate Professor of Clinical Surgery, College of Physicians and Surgeons, Columbia University; Associate Visiting Surgeon, Presbyterian Hospital, New York, N. Y. Cloth. Pp. 840, with 287 illustrations. Philadelphia, 1949, W. B. Saunders Company. $12.

Present advances in antibacterial therapy have greatly influenced the management of surgical infections. The sulfonamides and the antibiotics have made extensive surgical procedures safe that were previously impossible, and they have modified the extent of surgery necessary in other conditions. This book presents a thorough review of the prin-

ciples of treatment of surgical infections, emphasizing the changes in therapy brought about by these agents. The management of surgical infections is discussed not only from the point of view of the anatomic changes present, but particularly from the standpoint of directing specific therapy toward the removal of the etiologic agent.

The sections discussing acute and chronic gangrene are, of course, excellent. The review of the treatment of infected wounds is more complete than that available in any other single volume.

The literature is reviewed completely on each subject and many illustrated cases are presented.

The book provides an extensive discussion of the clinical uses of bacitracin, developed in the author's laboratory. In his enthusiasm for this very valuable drug, however, the author fails to discuss the dangers of its parenteral administration.

While this volume is primarily a reference book, it discusses from a practical point of view the problems of surgical infections that are frequently seen in clinical practice.

British Surgical Practice. Under the general editorship of Sir Ernest Rock Carling, F.R.C.S., F.R.C.P., Consulting Surgeon, Westminster Hospital, and J. Patterson Ross, M.S., F.R.C.S., Surgeon and Director of Surgical Clinical Unit, St. Bartholomew's Hospital; Professor of Surgery, University of London. Vol. IV. Cloth. St. Louis, 1948, The C. V. Mosby Company. $15.

Volume IV of this splendid series continues to be of the same type of character as the others. The illustrations are excellent and are profuse. The text is concise and well done. The chapter on fractures is particularly good as are the chapters on aspiration biopsy, which is excellently illustrated, and on injuries of the hand. It is regretted, however, that in the consideration of herpes zoster the extremely simple and yet effective procedure of interrupting the sympathetic impulses with procaine is not discussed.

British Surgical Practice. Under the general editorship of Sir Ernest Rock Carling, F.R.C.S., F.R.C.P., Consulting Surgeon, Westminster Hospital, and J. Patterson Ross, M.S., F.R.C.S., Surgeon and Director of Surgical Clinical Unit, St. Bartholomew's Hospital; Professor of Surgery, University of London. Vol. V. Cloth. St. Louis, 1948, The C. V. Mosby Company. $15.

Volume V is the same type as the previous volumes of this system of surgery. It is well illustrated. A consideration of the various subjects from Hodgkin's disease to lymphogranuloma inguinale is done concisely and in a lucid manner. It is of interest to a reviewer in the United States that so much space is devoted to tuberculous arthritis, which is a relatively rare condition in this country. In addition to the profuse number of black and white illustrations, there are also a large number of excellent colored illustrations which add materially to the value of the book.